

EVALUATION OF THE STABILITY OF LATANOPROST IN DIFFERENT LIQUID VEHICLES FOR TOPICAL APPLICATION

Aim of the study

The aim is to present results about the stability of latanoprost (supplier: Fagron, batch num.: L13070022) at total time of 90 days in different vehicles (70% ethanol solution, Espumil™ and Espumax®) on 2 conditions; refrigerator and climatic chamber.

Plan of work

- Vehicular latanoprost 0.05% in 3 types of vehicles: 70% ethanol solution (E), Espumil® (L) and Espumax (X). (E, X and L; 2nd letter on samples labelling).
- Storage of the samples using 2 conditions (Refrigerator: N) and (climatic chamber at 25 °C: C) (N and C; 1st letter on samples labelling).
- Samples were placed on freezer at -25 °C at the different times listed in the following table:

Date	SAMPLES TO BE PLACED ON FREEZER					
Tue June 10th	----	----	----	----	----	----
Wed June 11th	NE 1	NL 1	NX 1	CE 1	CL 1	CX 1
Fri June 13th	NE 3	NL 3	NX 3	CE 3	CL 3	CX 3
Thu June 17th	NE 7	NL 7	NX 7	CE 7	CL 7	CX 7
Wed June 25th	NE 15	NL 15	NX 15	CE 15	CL 15	CX 15
Thu July 10th	NE 30	NL 30	NX 30	CE 30	CL 30	CX 30
Fri August 8th	NE 60	NL 60	NX 60	CE 60	CL 60	CX 60
Mon September 1st	NE 90	NL 90	NX 90	CE 90	CL 90	CX 90

- Titration of latanoprost from the different samples previously thawed. We used USP method, modified.

Results

See the attached table which summarize the results + auxiliary tables wherein is specified that all the readings were carried out in duplicate, as well as a list of peak integration corresponding to Latanoprost (supplier: Fagron, batch num.: L13070022). By reading these tables we can give the following conclusions:

1. Latanoprost (supplier: Fagron, batch num.: L13070022) 0.05% remain stable at least 90 days (end point planned for this study), without showing peaks of deterioration, when we prepare it in a 70% ethanol solution and in Espumax®, whether it is conserved at room temperature (in this case, in a climatic chamber at 25 °C) or if it is refrigerated, in refrigerator, so for practical purposes the recommendation to keep refrigerated could be avoided.
2. Latanoprost (supplier: Fagron, batch num.: L13070022) 0.05% in Espumil™ shows deterioration in the order of 4% (samples stored in refrigerator) and in the order of 13-14% (samples stored at room temperature) at t90 days. Validity time (t90) for samples stored at room temperature should not exceed 60 days, or recommend their storage in a refrigerator if you want to extend already stated t90 to 90 days.

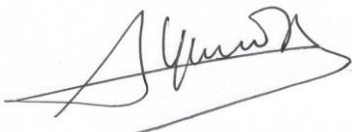
Exci- pient	Condi- tions	Subject	Times							
			Initial	1 day	3 days	7 days	15 days	30 days	60 days	90 days
Ethanol	Refrigerator	Area	5417,94	5400,14	5352,01	5381,74	5384,68	5395,49	5383,7	5375,07
		% rel. init	100,00%	99,67%	98,78%	99,33%	99,39%	99,59%	99,37%	99,21%
	Climatic chamber	Area	5417,94	5406,91	5361,17	5441,22	5405,89	5395,87	5390,67	5421,3
		% rel. init	100,00%	99,80%	98,95%	100,43%	99,78%	99,59%	99,50%	100,06%
Espumil	Refrigerator	Area	5430,66	5426,41	5348,82	5357,53	5342,69	5291,37	5280,54	5209,76
		% rel. init	100,00%	99,92%	98,49%	98,65%	98,38%	97,44%	97,24%	95,93%
	Climatic chamber	Area	5430,66	5370,12	5394,23	5314,89	5312,2	5212,92	4974,78	4712,38
		% rel. init	100,00%	98,89%	99,33%	97,87%	97,82%	95,99%	91,61%	86,77%
Espumax	Refrigerator	Area	5276,53	5254,23	5282,7	5266,89	5286,64	5268,45	5254,2	5260,71
		% rel. init	100,00%	99,58%	100,12%	99,82%	100,19%	99,85%	99,58%	99,70%
	Climatic chamber	Area	5276,53	5354,05	5380	5316,82	5296,83	5324,8	5419,78	5372,64
		% rel. init	100,00%	101,47%	101,96%	100,76%	100,38%	100,91%	102,71%	101,82%

The results (% of latanoprost found at the different times and sampling conditions) are expressed as a percentage of peak integration corresponding to latanoprost in chromatograms obtained at different sampling times relative to its area at time zero (initial).

Relation of areas				
Sample	Inject. 1	Inject. 2	Average	CV(%)
NE0	5431,64	5404,24	5417,94	0,36%
NE1	5433,3	5366,97	5400,14	0,87%
NE3	5323,6	5380,42	5352,01	0,75%
NE7	5406,08	5357,39	5381,74	0,64%
NE15	5394,08	5375,27	5384,68	0,25%
NE30	5388,25	5402,73	5395,49	0,19%
NE59	5383,08	5384,32	5383,70	0,02%
NE90	5383	5367,13	5375,07	0,21%
CE1	5392,67	5406,91	5399,79	0,19%
CE3	5366,93	5361,17	5364,05	0,08%
CE7	5418,9	5441,22	5430,06	0,29%
CE15	5351,75	5405,89	5378,82	0,71%
CE30	5436,29	5395,87	5416,08	0,53%
CE59	5394,21	5387,12	5390,67	0,09%
CE90	5410,07	5432,53	5421,30	0,29%

Relation of areas				
Sample	Inject. 1	Inject. 2	Average	CV(%)
NL0	5421,21	5440,11	5430,66	0,25%
NL1	5377,12	5475,7	5426,41	1,28%
NL3	5416,53	5281,11	5348,82	1,79%
NL7	5393,45	5321,6	5357,53	0,95%
NL15	5322,72	5362,65	5342,69	0,53%
NL30	5290,24	5292,5	5291,37	0,03%
NL59	5311,72	5249,35	5280,54	0,84%
NL90	5265,54	5153,97	5209,76	1,51%
CL1	5368,26	5371,98	5370,12	0,05%
CL3	5360,33	5428,13	5394,23	0,89%
CL7	5358	5271,77	5314,89	1,15%
CL15	5296,84	5327,55	5312,20	0,41%
CL30	5263,99	5161,85	5212,92	1,39%
CL59	4926,68	5022,87	4974,78	1,37%
CL90	4691,94	4732,81	4712,38	0,61%

Relation of areas				
Sample	Inject. 1	Inject. 2	Average	CV(%)
NX0	5290,81	5262,25	5276,53	0,38%
NX1	5265,29	5243,17	5254,23	0,30%
NX3	5262,93	5302,47	5282,70	0,53%
NX7	5234,25	5299,53	5266,89	0,88%
NX15	5279,71	5293,56	5286,64	0,19%
NX30	5245,4	5291,5	5268,45	0,62%
NX59	5266,23	5242,17	5254,20	0,32%
NX90	5254,55	5266,86	5260,71	0,17%
CX1	5357,68	5350,41	5354,05	0,10%
CX3	5353,04	5406,96	5380,00	0,71%
CX7	5295,76	5337,87	5316,82	0,56%
CX15	5315,81	5277,84	5296,83	0,51%
CX30	5309,46	5340,13	5324,80	0,41%
CX59	5464,09	5375,46	5419,78	1,16%
CX90	5391,98	5353,3	5372,64	0,51%



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