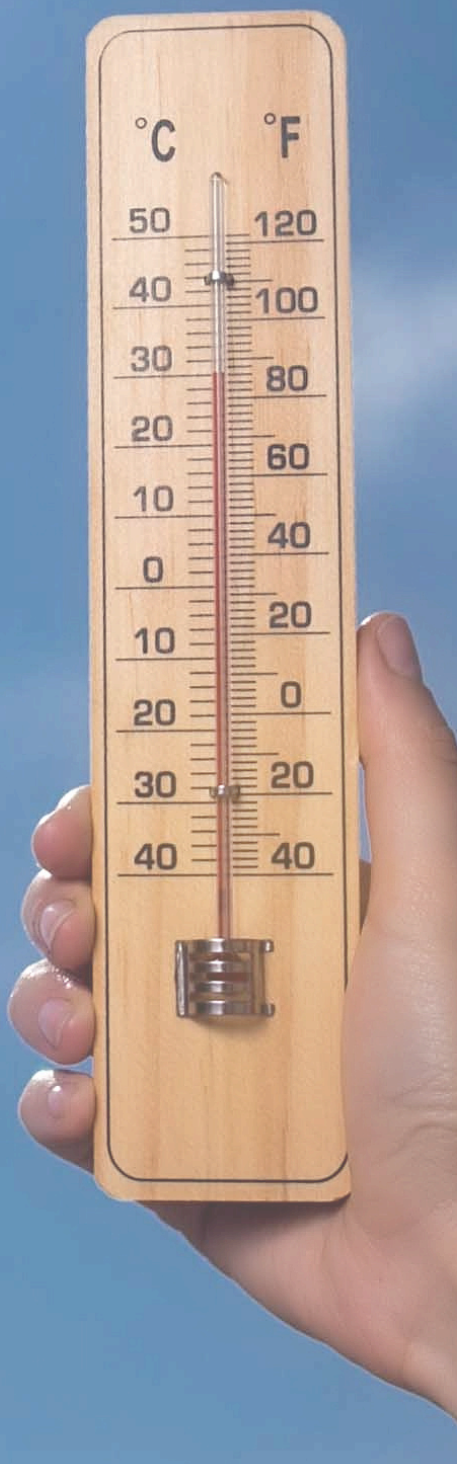
HEAT STRESS AND OPHTHALMIC MEDICATION STABILITY

Quality, Stability, and Patient Safety During Warm-Weather Shipping

At Massey Drugs, we understand that compounded ophthalmic medications shipped during the summer months may occasionally arrive warm due to elevated outdoor temperatures, hot delivery vehicles, or melted ice packs during transit. Because many ophthalmic formulations are refrigerated, this can understandably raise concerns for both prescribers and patients.

To better evaluate real-world shipping conditions, Massey Drugs commissioned third-party controlled heat stress studies on several commonly prescribed ophthalmic formulations to assess chemical stability under prolonged elevated temperature exposure.

To help reduce patient concern and confusion, each shipment includes instructions explaining that ophthalmic medications may occasionally arrive warm during summer transit and outlining when patients should contact the pharmacy regarding appearance or quality concerns.



How Heat Stress Testing Was Performed

- A portion of each sample was refrigerated while another portion was exposed to approximately 150°F (65°C) for up to 7 days to simulate extreme shipping and transit conditions.
- Samples were analyzed on Days 1, 2, 3, 4, and 7 using stability-indicating assays and compared against refrigerated control samples.
- Acceptance criteria for stability: 90%–110% potency remaining.

Massey Drugs

We Compound Solutions

Ophthalmic Formulations Evaluated

FORMULATION	HEAT STRESS STUDY RESULT
Losartan Ophthalmic Solution	**Chemically stable through 7 days at 150°F**
Prednisolone/Moxifloxacin/Bromfenac	**Chemically stable through 7 days at 150°F**
5-Fluorouracil Ophthalmic Solution	**Chemically stable through 7 days at 150°F**
Timolol/Brimonidine/Dorzolamide/Bimatoprost	**Chemically stable through 7 days at 150°F**
Atropine Ophthalmic Solution	**Chemically stable through 7 days at 150°F**
Naltrexone Ophthalmic Solution	**Chemically stable through 4 days at 150°F**

These studies were designed to evaluate whether temporary heat exposure during shipment necessarily compromises medication stability.

Our Commitment to Quality

Massey Drugs performs ongoing evaluation of compounded formulations with patient safety, medication integrity, and prescriber confidence in mind.

While we continue to recommend refrigerated or room temperature storage upon delivery when indicated, these studies help demonstrate that temporary heat exposure during shipment does not necessarily mean the medication has been compromised.

We understand the importance of preserving medication quality from the time a prescription leaves our pharmacy until it reaches the patient.

For questions regarding ophthalmic formulation stability or shipping procedures, please contact Massey Drugs at 833.540.3500.

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Analytical Laboratory Report

365 Day Stability of Losartan 0.8 mg/mL Ophthalmic Solution

Client **Date:** 9/8/2025

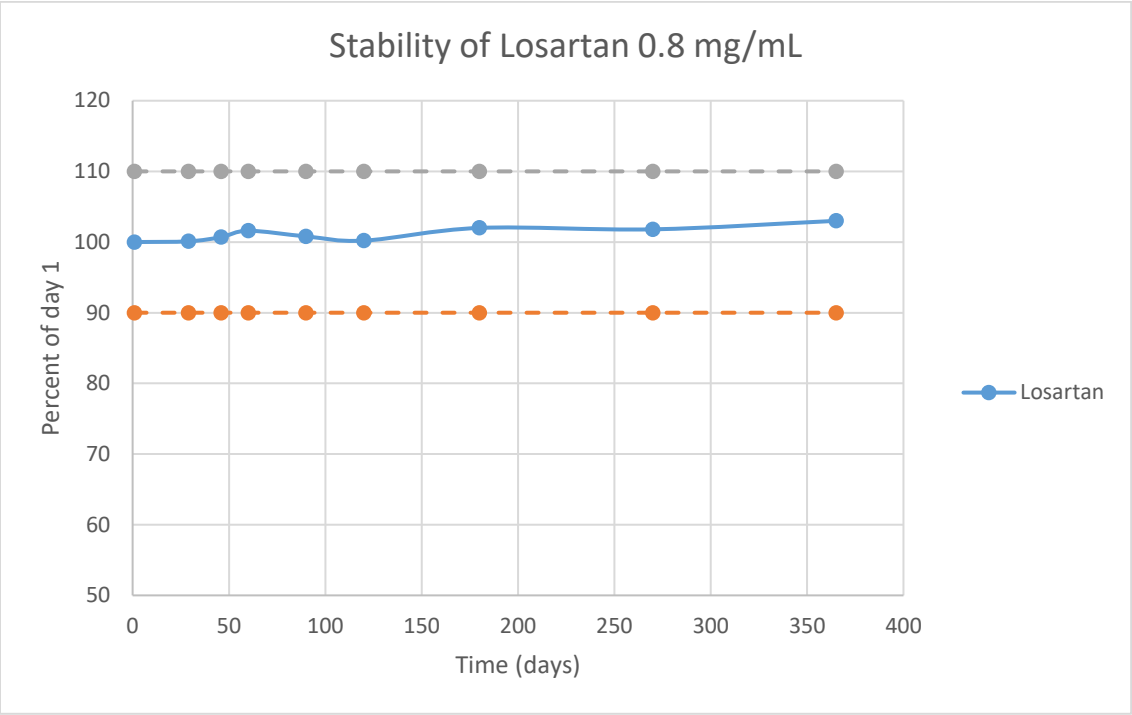
Massey Drugs
3501 Cloverdale Rd
Florence AL 35633
Dr. Brad Bowling

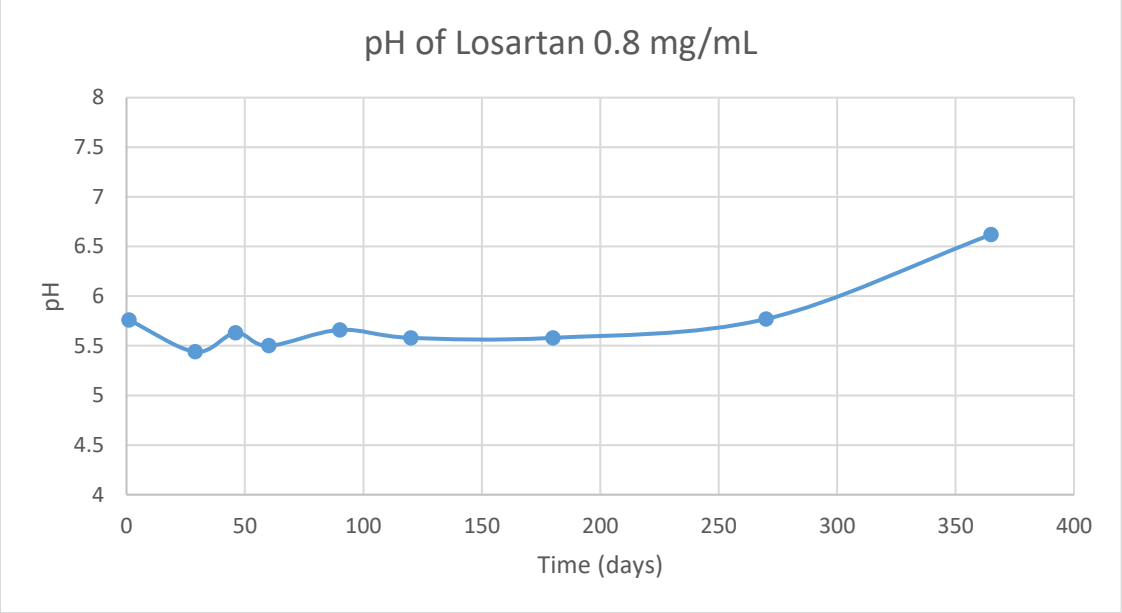
Scope: Determine the 365-day stability and pH of Losartan 0.8 mg/mL Ophthalmic solution stored refrigerated for 180 days then at room temperature through day 365.

Experimental: Sponsor supplied a solution of Losartan 0.8 mg/mL as the sample which was stored refrigerated (2-8°C). Triplicate samples taken from the vial on days 1, 29, 46, 60, 90, 180, 270, and 365 and were assayed using a high-performance liquid chromatographic stability indicating assay. Calibration standards prepared on each day of analysis were analyzed with each assay to quantitate the concentration of Losartan in the sample. The pH of the solution was also measured on each day of analysis.

Results: The attached graphs show the amount of Losartan 0.8 mg/mL as a percentage of day 1 concentration remaining in the sample as a function of time. The dotted lines on the stability graph represent the upper and lower allowed limits (± 10%) for drug stability. Each point represents the average of three samples. The second graph shows the measured pH of the formulation over the course of the study.

Conclusion: Losartan 0.8 mg/mL Ophthalmic solution when stored at refrigerated temperature from day 1- 180 then at room temperature through day 365 was determined to be stable. An increase in the pH between day 270 and 365 was observed.





Greg Gorman, Ph.D.

Professor and Laboratory Director, PSRI

Controlled Heat Studies (for summer shipping)

Pred/Moxi/Brom HEAT 1 WEEK
Losartan HEAT 1 WEEK
Naltrexone HEAT 1 WEEK
Fluorouracil HEAT 1 WEEK
Tim/Brim/Dor/Bimat HEAT 1 WEEK
Atropine HEAT 1 WEEK

Heat stress studies:
A portiopn of each samples as received from sponsor was stored in the refrigerator and the remaining sample was stored at approximately 150 F (65 C) for up to 7 days.
A representative portion from each were assayed at on days 1, 2, 3, 4, 7. Results reported for heat strees sample as percsnet or refrigerated sample.

Summary	% of Room temp sample		
	pred	**brom**	**mox**
Day 0	100	100	100
Day 1	99.9	100.1	98.9
Day 2	101.4	100.5	100.8
Day 3	104.5	103.6	100.1
Day 4	102	101.9	100.7
Day 7	99.4	98.6	95.4

Orange submitted sample

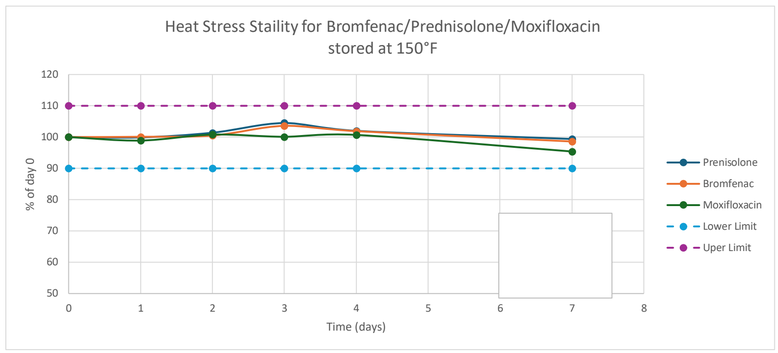
API	% of standard
Prednisolone	98.56
Bromfenac	96.05
Moxifloxacin	97.2

day	lower limit	upper limit
0	90	110
1	90	110
2	90	110
3	90	110
4	90	110
7	90	110

#VALUE!

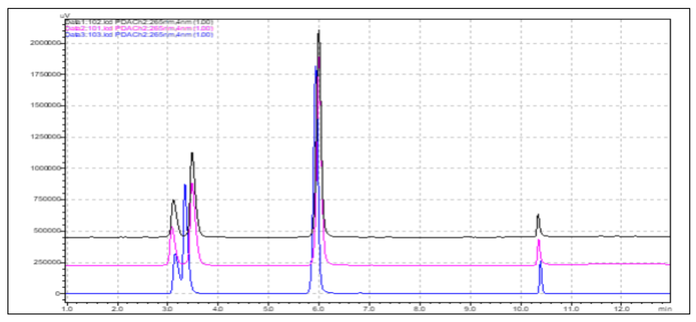
From Left to right: 7 days at: room temp, 150F, sample submitted

Slt discoloration when stored at 150F for 7 days, but less than submitted sample

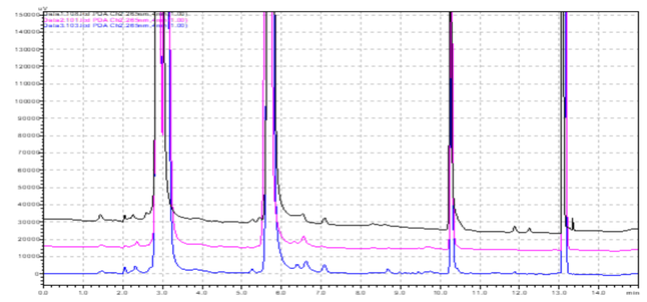


Conclusion

Based on the data from this study the formualtion containing
Prednisolone, Bromfenac and Moxifloxacin was determined to be chemically stable for at least 7



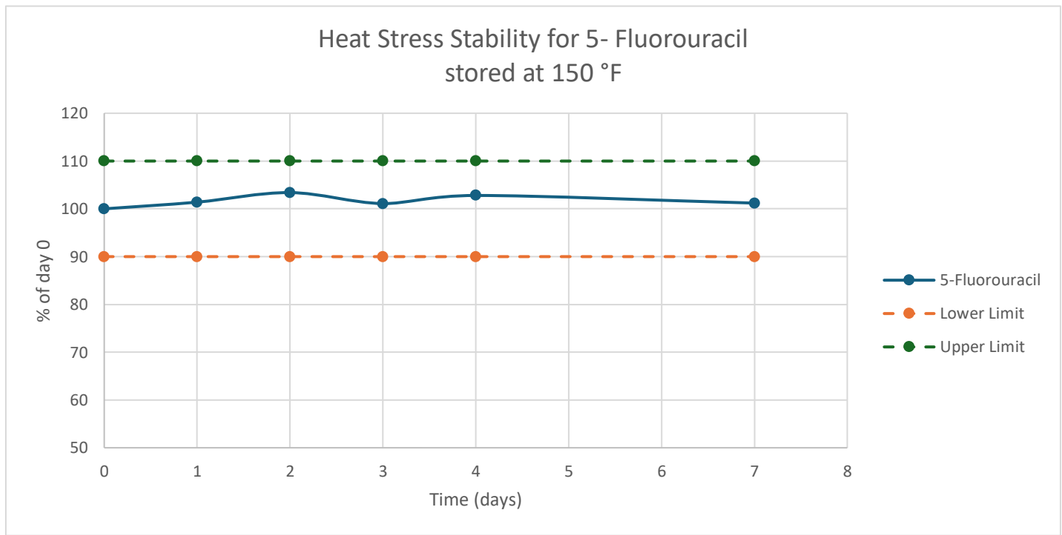
HPLC chromatogram at 265 nm, Room temp sample (top black line)
7 days heated to approx. 65 C (pink middle) and orange sample (blue bottom)



Expanded HPLC chromatogram from above

5-FU (1%)	% of Refrigerated Sample
Day 0 (pre heat exposure)	100
Day 1	101.4
Day 2	103.4
Day 3	101.1
Day 4	102.8
Day 7	101.2

day	lower limit	upper limit
0	90	110
1	90	110
2	90	110
3	90	110
4	90	110
7	90	110

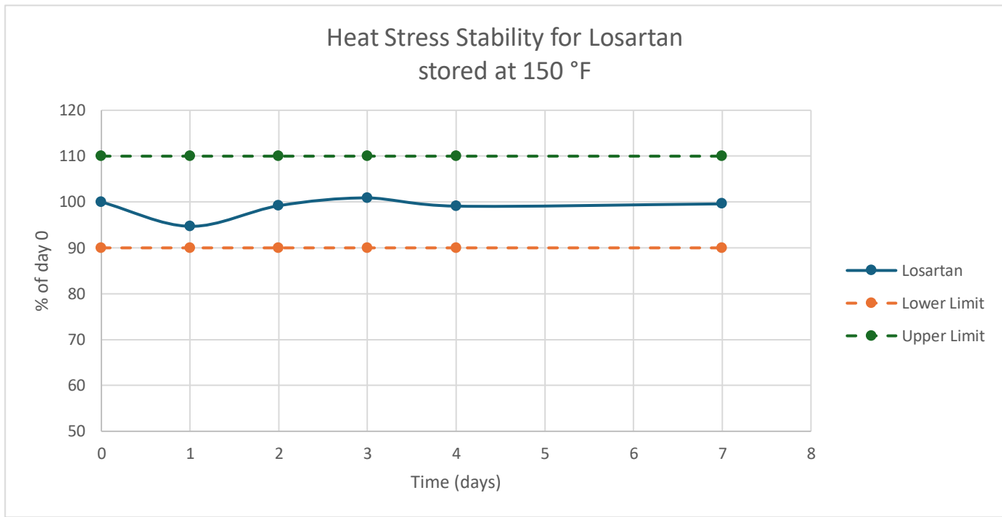


Conclusion

Based on the data from this study the formualtion containing
5-Fluorouracil was determined to be chemically stable for at least 7 days when stored at 150°F

Losartan	% of Refrigerated Sample
Day 0	100
Day 1	94.7
Day 2	99.2
Day 3	100.9
Day 4	99.1
Day 7	99.6

day	lower limit	upper limit
0	90	110
1	90	110
2	90	110
3	90	110
4	90	110
7	90	110

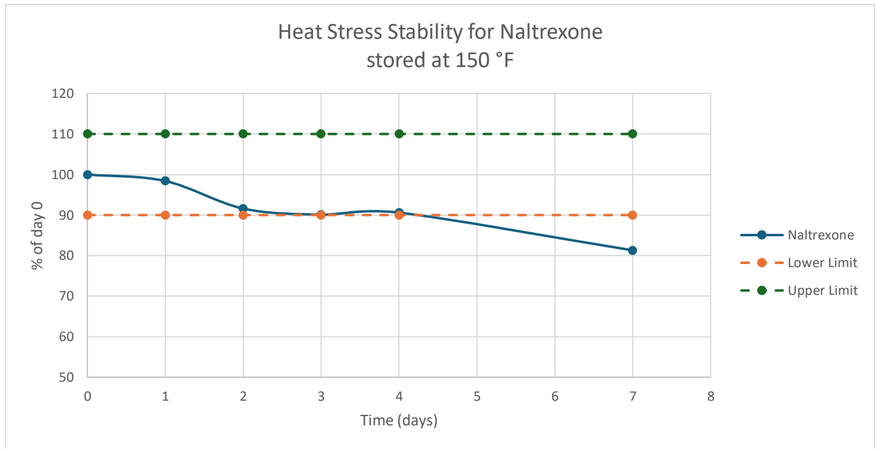


Conclusion

Based on the data from this study the formualtion containing
Losartan was determined to be chemically stable for at least 7 days when stored at 150°F

Naltrexone	% of Refrigerated Sample
Day 0	**100**
Day 1	98.4
Day 2	91.6
Day 3	90.1
Day 4	90.6
Day 7	81.3

day	lower limit	upper limit
0	90	110
1	90	110
2	90	110
3	90	110
4	90	110
7	90	110

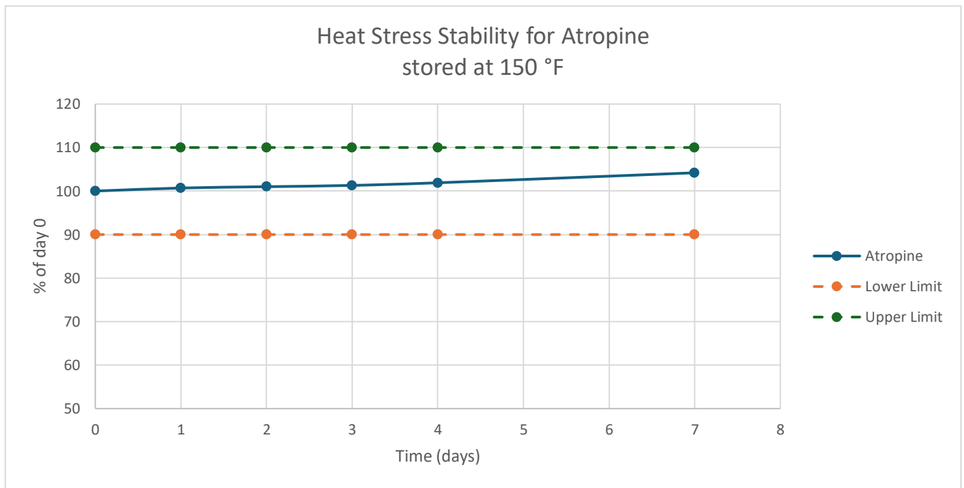


Conclusion

Based on the data from this study the formualtion containing
naltrexone was determined to be chemically stable for 4 days when stored at 150°F.

Atropine	% of refrigerated Sample
Day 0	100
Day 1	100.7
Day 2	101
Day 3	101.3
Day 4	101.9
Day 7	104.2

day	lower limit	upper limit
0	90	110
1	90	110
2	90	110
3	90	110
4	90	110
7	90	110

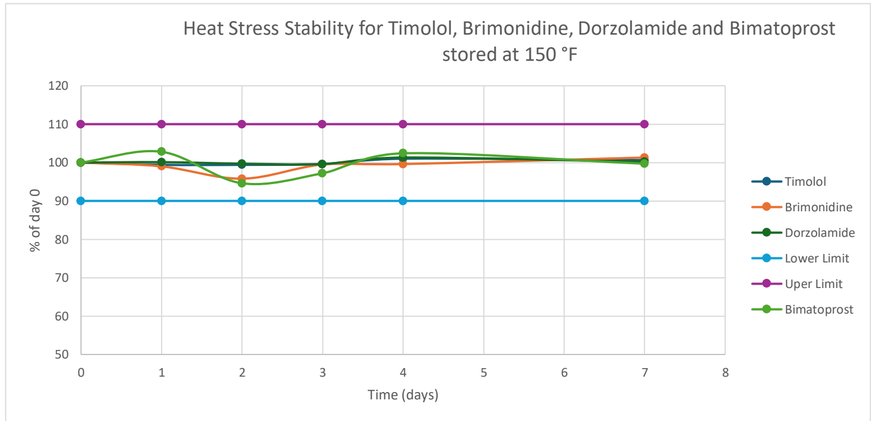


Conclusion

Based on the data from this study the formualtion containing
Atropine was determined to be chemically stable for at least 7 days when stored at 150°F

% of Refrigerated sample						
Sample	**Day 0**	**Day 1**	**Day 2**	**Day 3**	**Day 4**	**Day 7**
Timolol	100	99.4	99.4	99.6	101	100.6
Brimonidine	100	99	95.8	99.5	99.6	101.3
Dorzolamide	100	100.1	99.7	99.6	101.3	100.2
Bimatoprost	100	102.8	94.6	97.2	102.4	99.7

day	lower limit	upper limit
0	90	110
1	90	110
2	90	110
3	90	110
4	90	110
7	90	110



Conclusion

Based on the data from this study the formualtion containing
Timolol, Brimonidine, Dorzolamide, and Bimatoprost was determined to be chemically stable for at least 7 days when stored at 150°F