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Development and Validation of HPLC Assay Method for Stability Testing of a High-Potency Diclofenac Sodium Gel

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Purpose

The objective of this study was to investigate the stability of Diclofenac sodium in VersaPro™ gel base. The beyond-use date information is useful to support preparation of this formulation by compounding pharmacies.

Additionally, a selective HPLC assay method for Diclofenac sodium in VersaPro™ gel base was developed and validated for use in the stability analyses.

Assay

Table 1. HPLC Assay Method

Column:	Agilent Zorbax Eclipse Plus C18, 150x3.0 mm, 3.5 µm			
Mobile Phases:	A: 38mM Sodium Phosphate Buffer, pH 2.6 in Water			
	B: Acetonitrile			
	Time (minutes)	%A	%B	Flow (mL/min)
Gradient:	0.0	92	8	0.60
	2.0	92	8	0.60
	14.0	25	75	0.60
	19.5	25	75	0.65
	19.51	92	8	0.65
	20.0	92	8	0.60
Wavelength:	Time (minutes)	Wavelength (nm)		
	0.0	215		
	9.8	285		
Column Temp:	30°C			
Flow Rate:	0.60-0.65 mL/min			
Run Time:	24 minutes			
Injection Vol.:	5 µL			
Diluent:	70:30 / Methanol: Water			
Target Conc.:	0.5 mg/mL of 10% Diclofenac sodium formulation			

Table 2. Assay Method Validation Results

Parameters	Results
System Suitability:	Peak Area RSD ≤ 0.2%; TF ≤ 1.3; Check Standard Recovery = 99.8-100.4%
Selectivity:	Suitable under stressed conditions[1]
Sensitivity:	S/N > 500 at 20% Target
Linearity:	R^2 = 0.9999 for 80-120% Target
Accuracy:	Recovery = 100.5-101.3% for 80-120% Target
Precision:	RSD = 0.2% (n=9)
Robustness:	Recovery = 99.7-100.6%

1: degraded by light, heat, acid, base, and oxidation

Method

Formulation: 10% Diclofenac sodium in VersaPro™ gel base

- 450g batches (n=3) prepared using proprietary method
- Batch uniformity (BU) by stratified sampling plan
- Each batch divided into 6 Unguator® jars containing ~70g

Stability Storage: 4°C, 25°C/60%RH, and 40°C/75%RH

- 2 closed 100 ml jars per batch per condition
- Sampled at 7 days (40°C); 30, 60, 90 days (25°C and 4°C)

Diclofenac Assay: Dionex Ultimate 3000 HPLC (Table 1)

- Validated for intended use (Table 2)
- BU (n=10) and stability samples (n=2)
- Samples dissolved in diluent and filtered before analysis

Results

Method validation results (Table 2) indicated sufficient method performance (Figure 1) for the stability study (Figure 2).

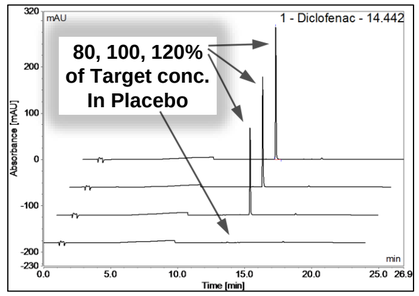

Figure 1. Accuracy Sample Comparison

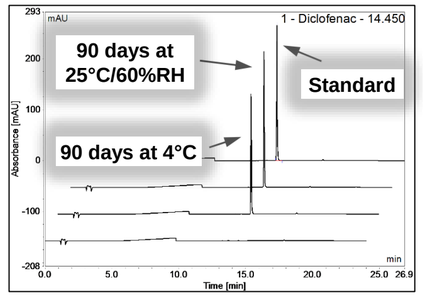

Figure 2. Stability Sample Comparison

Batch uniformity test results (Table 3) showed RSDs for all 3 batches (0.9-1.5%) below the specification limit of 6%.

Table 3. Batch Uniformity Potency Results (% Label Claim)

(n=10)	Batch A	Batch B	Batch C	All Batches
High	101.8%	101.7%	100.1%	101.8%
Low	97.4%	97.1%	97.1%	97.1%
Average	99.0%	98.7%	99.0%	98.9%
RSD	1.5%	1.4%	0.9%	1.3%

Results

Stability results (Figure 3) showed an 11.2% decrease in Diclofenac sodium potency after 7 days at 40°C/75%RH, whereas potency for the 4°C and 25°C/60%RH samples was ±2% of initial results after 30, 60, and 90 days of storage.

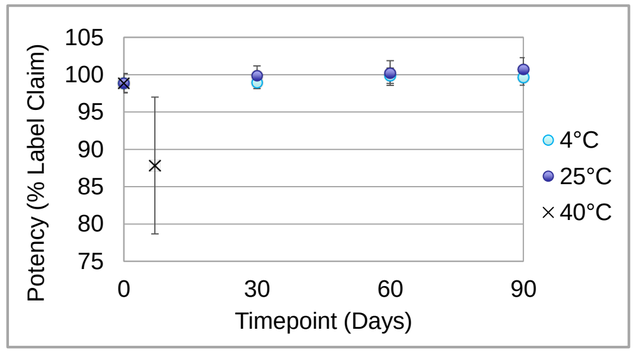

Figure 3. Stability Results Summary

A visual comparison of 7-day 40°C/75%RH sample to 30-day samples (Figure 4) indicated a physical change occurred in the 7-day sample, likely due to the elevated storage temperature.

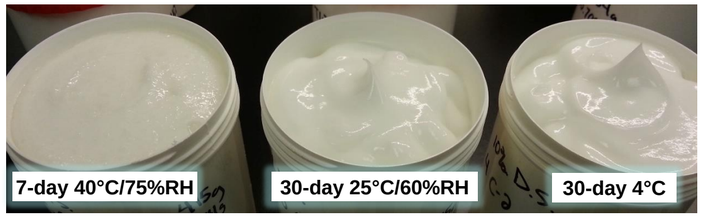

Figure 4. Stability Sample Appearance

Conclusions

A selective, sensitive, accurate, precise and reliable HPLC method was developed and validated for stability testing of the high-potency gel-based Diclofenac sodium formulation.

Results of stability testing showed that the Diclofenac sodium formulation was stable for up to 90 days at 4°C and 25°C/60%RH but less than 7 days at 40°C/75%RH.

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