APPLICATION BRIEF

Pharmaceutical

Monitoring Basic Hydrolysis By-Products of Loratadine by UHPLC/SQ MS

Drugs can undergo degradation during storage. We studied the breakdown of the antihistamine drug loratadine, under accelerated degradation conditions and identified the hydrolysis products using UHPLC/SQ MS. Loratadine is commercially used in tablet or syrup form and contains an ester bond that is susceptible to hydrolysis.

Experimental Conditions

Target Analytes: Desloratadine, loratadine

Sample Preparation Conditions

A 10 mg tablet of a commercial product containing loratadine was crushed into a 50 mL volumetric flask and brought to volume with ethanol. The flask was shaken, vortexed for ~2 min, 1 mL of supernatant was filtered through a 0.45 micron filter. The filtered supernatant was diluted 1:10 in ethanol and 2 µL injected on column. Additionally, filtered supernatant (1 mL) was base hydrolyzed in NaOH (final concentration of NaOH was 0.25 N) overnight at ~95 °C and analyzed by UHPLC/SQ MS.

Liquid Chromatography Conditions

Pump Type:	PerkinElmer® Flexar™ FX-15
Column:	Grace® VisionHT™-HL column (2.1 mm x 50 mm, 1.9 µm)
Mobile Phase:	A: water containing 0.1% formic acid B: acetonitrile containing 0.1% formic acid
Flow Rate:	0.8 mL/min with a post column split of 0.4 mL/min into MS
Injection Volume:	1 µL/min in partial fill mode

Gradient:

Time (min)	%A	%B
0	90	10
5	50	50
3	50	50

Mass Spectrometer Conditions

Ionization:	Ultraspray™ ESI – Positive mode
Scan Range:	100-1500 m/z
Scan Rate:	2000 u/sec
Capillary Exit Voltage:	100 V

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Results

Figure 1 shows the TIC of an over-the-counter tablet containing loratadine. The mass spectrum of the major peak eluting at 3.6 min shows an electrospray mass spectrum consistent with the loratadine structure (Figure 2).

The loratadine sample subjected to basic hydrolysis showed two by-product peaks at retention times ~1 and 2.7 min (Figure 3A). The peak at ~1 min shows a mass spectrum that matched a known degradation product called desloratadine (Figure 3B) obtained from the parent drug. The peak at ~2.7 min corresponded to a mass spectrum of a proposed structure (Figure 4) which may most likely form with rearrangement reactions.

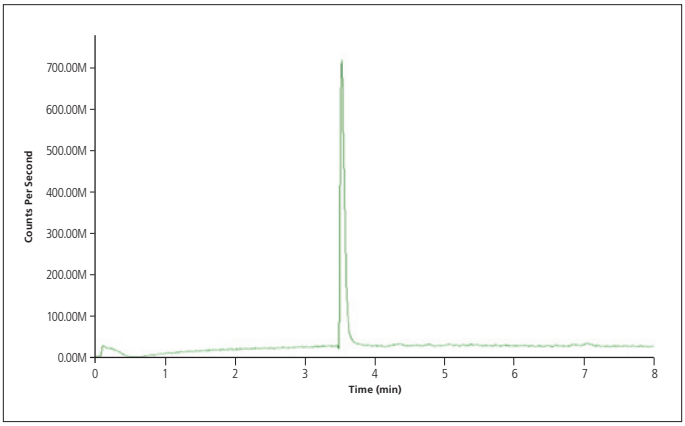

Figure 1. TIC of loratadine sample.

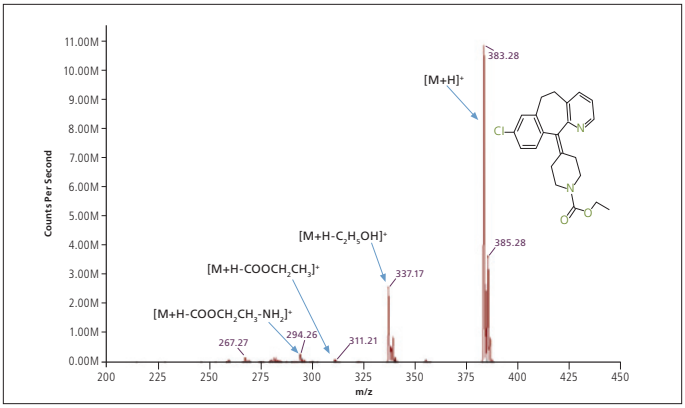

Figure 2. Mass spectrum of loratadine eluting at 3.6 min.

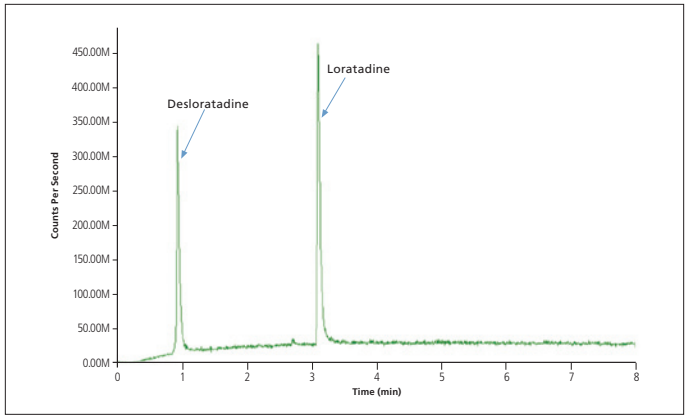

Figure 3A. TIC of the basic hydrolyzed loratadine sample.

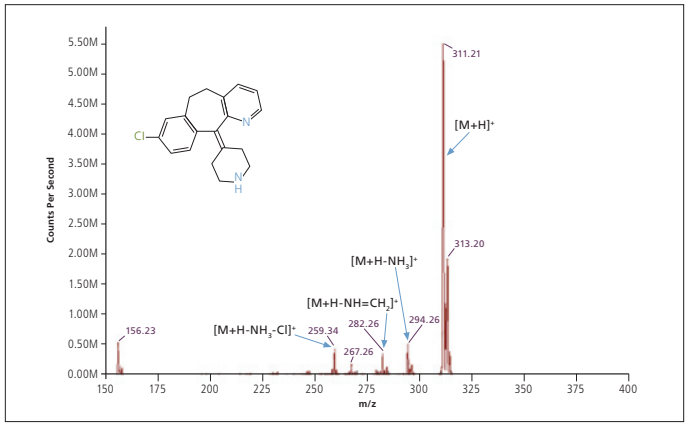

Figure 3B. Mass spectrum of desloratadine, a by-product of basic hydrolysis of loratadine eluting at retention time ~1 min.

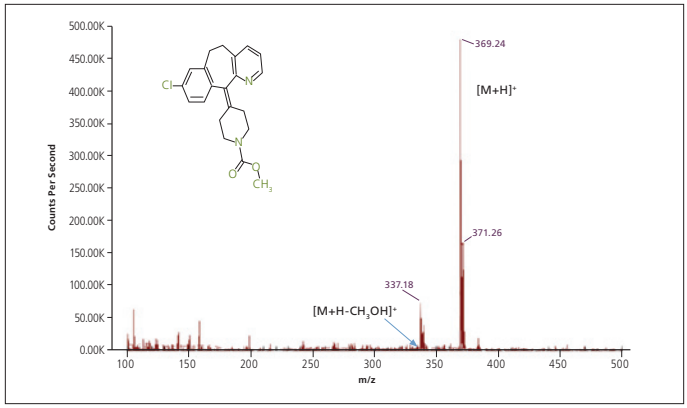

Figure 4. Mass spectrum of a by-product of basic hydrolysis of loratadine eluting at retention time of ~2.7 min. The proposed structure (methyl 4-(8-chloro-5,6-dihydro-11*H*-benzo[5,6]cyclohepta[1,2-*b*]pyridin-11-ylidene) -1-piperidinecarboxylate) based on the mass spectrum may form with rearrangement reactions.

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