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i-Series LC-2050 / USP 41 monograph

Application News

Organic Impurity Analysis of Cetirizine Hydrochloride Drug Material Following USP Monograph

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User Benefits

- Two procedures (1 and 2) for organic impurities analysis of cetirizine hydrochloride following USP 41 monograph were performed on Shimadzu i-Series LC-2050 HPLC system.
- The results of testing solutions of cetirizine hydrochloride drug substance meet the suitability test requirements and show highly-sensitive HPLC analysis feature in the impurity profiling analysis.

■ Introduction

The profiling analysis of impurities in drug products is essential for ensuring product quality and consumer safety. Cetirizine (Fig. 1) is a non-sedating antihistamine, which is classified as a second-generation antihistamine. According to the USP 41[1] monograph for the organic impurity analysis of cetirizine hydrochloride, there are two procedures which can be applied for different types of impurities analysis. In this application note, these two analysis procedures were performed on Shimadzu i-series LC-2050 HPLC system for profiling analysis of organic impurities in cetirizine hydrochloride drug substance.

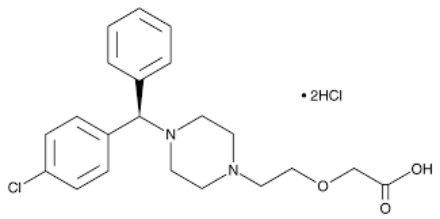

Figure 1. chemical structure of cetirizine hydrochloride

■ Experimental

Drug material and Chemicals

The cetirizine hydrochloride drug material used as the testing sample was provided by a collaboration laboratory. Tetrabutyl ammonium hydrogen sulfate, monobasic sodium phosphate monohydrate, dibasic sodium phosphate heptahydrate and sodium hydroxide were obtained from Sigma-Aldrich. Sulfuric acid (ACS reagent, > 51%) was supplied by J.T. Baker. Acetonitrile and methanol (LC grade) were purchased from Fisher.

Preparation of Solutions

According to Procedure 1 in the USP 41 monograph, a stock solution of 500 µg/mL was prepared using mobile phase as the diluent. The standard solutions of 4 µg/mL and 0.5 µg/mL were used for system suitability test.

For Procedure 2, buffer A was prepared from 2 g of tetrabutyl ammonium hydrogen sulfate and 3 g of monobasic sodium phosphate monohydrate in 1 L of pure water. The pH of buffer A was adjusted with 1 N of sodium hydroxide solution to a pH of 2.8 ± 0.05. Buffer A was used as mobile phase A. Buffer B was prepared from 1.4 g of monobasic sodium phosphate monohydrate and 2.7 g of dibasic sodium phosphate heptahydrate in 1 L of pure water. The pH of buffer B was adjusted with 1 N of sodium hydroxide to a pH 6.9 ± 0.1. Buffer B was mixed with acetonitrile at 1:1 (v/v) ratio as the diluent. The test sample solutions of 2 mg/mL and 2 µg/mL were prepared using the above prepared diluent.

Analytical conditions

The Shimadzu i-Series LC-2050 system was employed in this work. The details of HPLC analytical conditions are compiled into Table 1 & 2.

Table 1. Analytical conditions used in Procedure 1

Column	Shim-pack™ UC-Sil (250 x 4.6 mm, I.D. 5 µm), L3
Mobile Phase	ACN : H_2O : 1M H_2SO_4 = 93 : 6.6 : 0.4 (v/v/v)
Elution mode	Isocratic
Flow Rate	1.0 mL/min
Detector	UV 230 nm
Oven temp.	40°C
Injection Vol.	10 µL

Table 2. Analytical conditions used in Procedure 2

Column	Shim-pack GIST (250 x 4.6 mm, I.D. 5 µm), L1			
Mobile phase	A: Buffer A; B: Methanol			
Elution program	Time (min)	A (%)	B (%)	Flow rate (mL/min)
	0	58	42	1.2
	40	58	42	1.2
	68	20	80	1.5
	108	20	80	1.5
	110	58	42	1.2
	120	58	42	1.2
Detector	UV 232 nm			
Oven temp.	40 °C			
Injection vol.	10 µL			

■ Results and Discussion

Procedure 1

System suitability test: Following USP 41 monograph, the cetirizine hydrochloride solution of 0.5 µg/mL was used to test the repeatability. The cetirizine hydrochloride solution of 4 µg/mL was used for measuring tailing factor. The suitability test results are summarized in Table 3, which meet the system suitability requirements.

Impurity profiling: The cetirizine solution of 500 µg/mL was used for the impurity profiling analysis. The chromatogram (UV230 nm) is shown in Figure 2. The peak list is shown in Table 4. Three impurities stated in the USP 41 monograph were identified based on the RRT matching. In addition, six unknown impurities (Unk 1~Unk6) were detected and their area% were below 0.1%.

Procedure 2

System suitability test: Following the USP 41 monograph, cetirizine hydrochloride test solution of 2 µg/mL was used to determine the tailing factor, theoretical plates and the repeatability. The results are summarized in Table 3, indicating the system suitability requirements being met.

Table 3. System suitability test as required in USP 41

Procedure	Test factor	Conc. (µg/mL)	Acceptance Criteria	Values (n=6)	Results
1	Area %RSD	0.5	NMT 2.0%	0.55%	Pass
	RT %RSD	0.5	NMT 2.0%	0.06%	Pass
	Tailing factor	4	NMT 2	1.03	Pass
2	Area %RSD	2	NMT 5.0%	1.45%	Pass
	RT %RSD	2	NMT 5.0%	0.18%	Pass
	Tailing factor	2	NMT 2	0.929	Pass
	Theoretical plates	2	NLT 6000	47730	Pass

Impurity profiling: The cetirizine solution of 2 mg/mL was used for impurity profiling analysis. The chromatogram is shown in Figure 3. The impurity peaks are listed in Table 5. Five impurities stated in the USP 41 monograph were identified based on the RRT matching. In addition, five additional impurities (UnkA~UnkE) were detected, which area% were below 0.1% except Unk C (0.32%) and UnkD (0.112%).

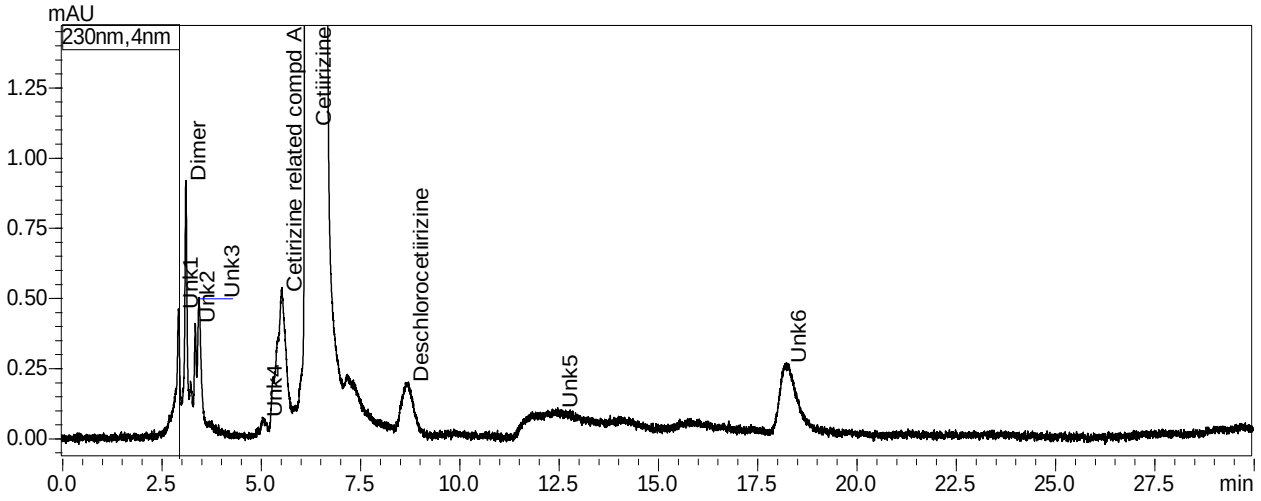

Figure 2. HPLC impurity profile of cetirizine testing solution (500 µg/mL) following Procedure 1 in USP 41

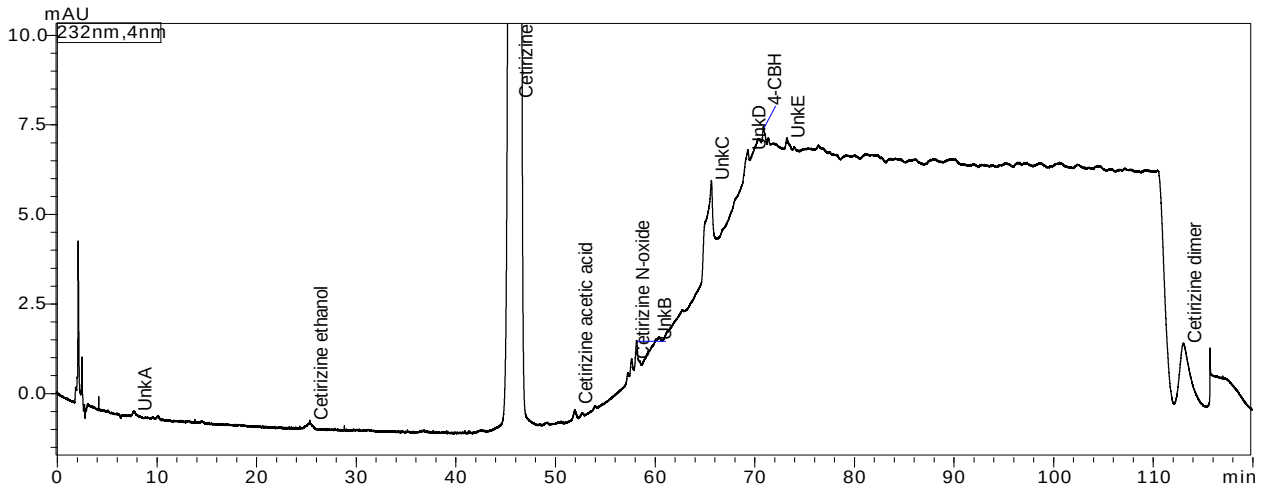

Figure 3. HPLC impurity profile of cetirizine testing solution (2 mg/mL) following Procedure 2 in USP 41

Table 4. Results of impurities in cetirizine testing solution (500 µg/mL) by Procdure1 in USP 41

Peak#	RT(min)	Area%	RRT	Compound
1	2.939	0.022	0.468	Unk1
2	3.128	0.037	0.498	Dimer
3	3.364	0.013	0.536	Unk2
4	3.459	0.027	0.551	Unk3
5	5.056	0.004	0.805	Unk4
6	5.544	0.074	0.883	Cetirizine related compound A
7	6.277	99.641	1.000	Cetirizine
8	8.733	0.032	1.391	Deschlorocetirizine
9	12.489	0.067	1.990	Unk5
10	18.24	0.073	2.906	Unk6
Total Impurities		0.359		

Table 5. Results of impurities in cetirizine testing solution (2 mg/mL) by Procedure 2 in USP 41

Peak#	RT(min)	Area%	RRT	Compound
1	7.779	0.011	0.169	UnkA
2	25.44	0.022	0.553	Cetirizine ethanol
3	46.029	98.86	1.000	Cetirizine
4	52.028	0.018	1.130	Cetirizine acetic acid
5	57.753	0.033	1.255	Cetirizine N-oxide
6	58.228	0.063	1.265	UnkB
7	65.74	0.32	1.428	UnkC
8	69.384	0.112	1.507	UnkD
9	70.961	0.073	1.542	4-CBH
10	73.321	0.023	1.593	UnkE
11	113.132	0.465	2.458	Cetirizine dimer
Total Impurities		1.14		

■ Conclusion

This study demonstrates the organic impurities analysis of cetirizine hydrochloride following USP 41 monographs / Cetirizine Hydrochloride method on Shimadzu LC-2050 i-series HPLC system. Both procedure 1 and procedure 2 were performed using a drug material obtained from manufacturer. The system suitability test results meet the requirements, and the impurity profile analysis of the testing samples shows highly-sensitive features, allowing detection of trace levels (<0.1%) of targeted impurities and unknown impurities.

■ Reference

1. USP (USP 41, Official from May 1, 2018) Official Monographs / Cetirizine Hydrochloride

■ Acknowledgement

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