SHIMADZU
Excellence in Science

Application News

Ultra High Performance Liquid Chromatograph Nexera™ FV

Online Dissolution Testing of Roxatidine Acetate Hydrochloride Extended-Release Capsules

K. Matsuoka, A. Tanabe

User Benefits

- Dissolution testing can be automated.
- The automatic sampling function enables testing with good reproducibility.
- The automatic dilution function improves work efficiency.

■ Introduction

Dissolution testing is conducted for formulation development, quality control, bioequivalence tests of generic drugs, etc. In dissolution testing, the dissolution properties of a drug product are checked under specific conditions for certain periods. Dissolution testing takes a lot of labor and time, since dissolution media must be sampled from multiple vessels every sampling time and analyzed.

Nexera FV is an HPLC system for online dissolution testing. It can automate the processes from sampling dissolution media, HPLC analysis, up to report output. By automating tasks that used to be conducted manually by operators, the system realizes labor saving and throughput improvement. In addition, automating tasks prevent human errors from whole processes.

This article introduces the workflow of online dissolution testing of roxatidine acetate hydrochloride extended-release capsules, using Nexera FV.

■ Online Dissolution Testing with Nexera FV

Fig. 1 shows a comparative example of the workflow of conventional method and online dissolution testing with Nexera FV. The Nexera FV system can automate sampling of dissolution medium at designated times, filtration, dilution, addition of internal standards, HPLC analysis, and report generation processes which had been conducted manually. Furthermore, the HPLC analytical conditions can be set easily by the dedicated software DT-Solution (Fig. 2), and a report summarizing multiple data such as the dissolution rate is prepared simultaneously with completion of the analysis (Fig. 3).

Nexera FV has two modes of analysis: direct injection mode to inject the dissolution media delivered from the dissolution tester directly to the HPLC, and fraction analysis mode to fractionate the dissolution media into vials and analyze them. The former is effective when an analysis is enough short to complete by the next sampling time. The latter is used in tests with short sampling intervals, and in cases where dilution or addition of internal standards is required.

Furthermore, the fraction analysis mode also makes it possible to conduct HPLC analyses between sampling intervals. As a result, the total time could be reduced by 35%.

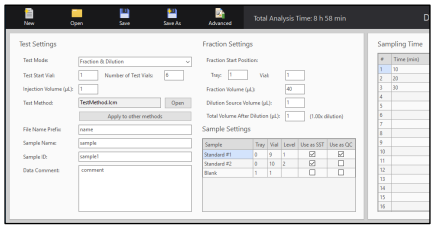


Fig. 2 DT-Solution Setting Window

Fig. 3 Multi-Data Report*1 Window

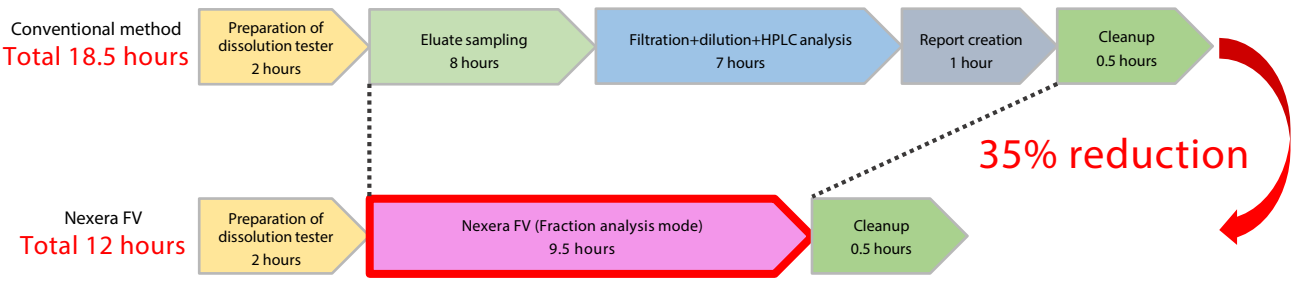


Fig. 1 Comparison of Workflow of Online Dissolution Testing*2

*1 Multi-Data Report is an optional function of LabSolutions™DB/CS to generate reports automatically.
*2 The time above is an example of roxatidine acetate hydrochloride extended-release capsules with a dissolution test of 8 hours and an HPLC analysis of 5.5 hours (42 analyses of 8 minutes each).

■ System Suitability Test

Table 1 shows the analytical conditions, and Fig. 4 shows the chromatogram of the standard roxatidine acetate hydrochloride. Table 2 then shows the results of the system suitability test. The analytical conditions were determined by referring to the test conditions listed in the Japanese Pharmacopoeia, 18th edition, "Roxatidine Acetate Hydrochloride Extended-Release Capsules". For reference, Table 3 shows the suitability requirements described in the Japanese Pharmacopoeia, 18th edition. The system suitability was confirmed by the repeated analyses at 42 mg/L standard solution (n=6) under the conditions shown in Table 1. Both the system performance and reproducibility meet requirements described in the 18th edition of the Japanese Pharmacopoeia.

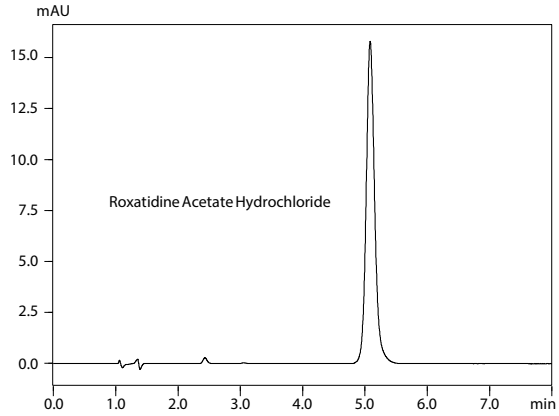


Fig. 4 Chromatogram of Standard Roxatidine Acetate Hydrochloride (42 mg/L)

Table 1 HPLC Conditions

Column	: Shim-pack™ VP-ODS*1 (150 mm × 4.6 mm I.D., 5 µm)
Mobile phase	: Water / Acetonitrile / Triethylamine / Acetic Acid = 340 : 60 : 2 : 1
Flow rate	: 0.8 mL/min
Column temp.	: 40 ˚C
Injection vol.	: 20 µL
Vial	: Shimadzu Vial, LC, 1.1 mL, Glass*2
Detection	: UV 274 nm

*1 P/N: 228-34937-91
*2 P/N: 228-21283-91

Table 3 System Suitability Test Requirements (Japanese Pharmacopoeia, 18th Edition)

System Repeatability	Area %RSD ≤ 1.0% *3
System Performance	Theoretical Plate Number ≥ 3000*4 and Symmetry Factor ≤ 2.0*4

*3 Condition: analyzing 100 µL of 42 mg/L standard solution repeatedly (n=6)
*4 Condition: analyzing 100 µL of 42 mg/L standard solution

Table 2 Results of System Suitability Test (42 mg/L)

	Retention Time (min)	System Reproducibility	System Performance	
		Area	Theoretical Plate Number	Symmetry Factor
1st	5.077	149282	7362	1.15
2nd	5.078	149485	7398	1.15
3rd	5.079	149358	7353	1.15
4th	5.082	249368	7372	1.15
5th	5.081	149885	7371	1.15
6th	5.083	149107	7372	1.15
Averages	5.08	149248	-	-
%RSD	0.05	0.15	-	-
Judgement		PASSED	PASSED	PASSED

■ Dissolution Test

Fig. 5 shows the chromatogram of the dissolution medium from commercially available roxatidine acetate hydrochloride extended-release capsules (labeled amount: 75 mg per capsule, dissolution time: 8 hours). Table 4 shows the dissolution conditions. HPLC analytical conditions are the same as those in Table 1. The conditions for dissolution and HPLC analysis were determined by referring to the test conditions listed in the Japanese Pharmacopoeia, 18th edition, "Roxatidine Acetate Hydrochloride Extended-Release Capsules". Fig. 6 shows the dissolution curve, Table 5 shows the results of the dissolution test, and Table 6 shows the tolerances for the dissolution test of roxatidine acetate hydrochloride extended-release capsules listed in the Japanese Pharmacopoeia, 18th edition, as reference values. In this test, we used sinkers for dissolution. The dissolution medium was automatically sampled and filtered at specified timing, automatically diluted 2 times with water using Nexera FV, and then analyzed.

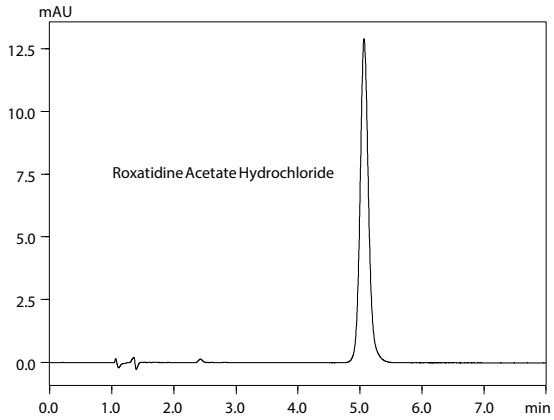
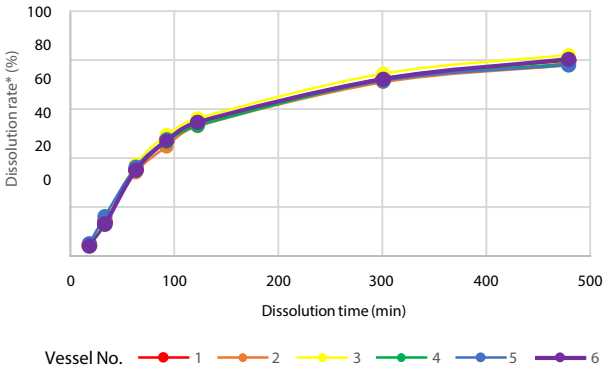


Fig. 5 Chromatogram of Roxatidine Acetate Hydrochloride Extended-Release Capsules (Dissolution Time of 8 Hours)

Table 4 Dissolution Conditions

System	: NTR-6600AST (TOYAMA SANGYO CO., LTD.)
Dissolution method	: Paddle
Dissolution media	: Pure water
Media volume	: 900 mL
Rotation speed	: 50 rpm
Bath temperature	: 37 ˚C
Total time	: 480 min
Sampling time	: 15, 30, 60, 90, 120, 300 and 480 min



* Dissolution rate (%) = Concentration (mg/L) × Media volume 0.9 (L) / Labeled amount 75 (mg) × 100

Fig. 6 Dissolution Curve

Table 6 Tolerances of the Dissolution Test (Japanese Pharmacopoeia, 18th Edition)

Time (min)	Results *
60	20 to 50%
90	35 to 65%
480	≥ 70%

* Condition: analyzing 100 µL of dissolution medium

■ Conclusion

Online dissolution test of roxatidine acetate hydrochloride extended-release capsules was carried out. The dissolution test was able to be carried out more easily than conventional methods. In this case, about 35% of the total time required for the entire processes was able to be reduced.

Table 5 Dissolution Rate of 75 mg Capsule (%)

Time (min) / Vessel No.	15	30	60	90	120	300	480
1	4.74	14.46	35.98	48.40	55.33	73.81	81.30
2	5.08	15.12	34.92	45.61	54.09	72.33	79.39
3	4.76	14.85	38.09	50.43	57.30	75.84	83.63
4	4.57	13.76	35.62	47.59	54.17	72.97	80.06
5	5.46	16.70	37.14	48.52	55.72	72.93	79.42
6	4.38	13.40	35.84	48.03	55.71	73.60	81.83
Judgement			PASSED	PASSED			PASSED

SHIMADZU
Shimadzu Corporation
Analytical & Measuring Instruments Division
Global Application Development Center

www.shimadzu.com/an/

01-00029-EN First Edition: Oct. 2021