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High Performance Liquid Chromatography Nexera™FV

Application News

On-line Dissolution Test of Loxoprofen Sodium Tablets

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User Benefits

- On-line dissolution test can significantly reduce the man-hours required from test solution sampling to HPLC analysis.
- Fraction analysis mode provides sampling of test solution at minimum 5-minute intervals and is expected to save labor and prevent human error.
- Direct injection analysis mode doesn't require fractionation vials, resulting in cost reduction.

■ Introduction

Disintegration tests and dissolution tests are specified by the Japanese Pharmacopoeia (JP) and the U.S. Pharmacopeia (USP). Nexera FV is an on-line HPLC system for automated dissolution testing of drug products. By connecting to a dissolution tester, the system can provide tablet loading, analysis of the test solution at each sampling time, calculation of dissolution rate, and preparation of report output automatically. This system eliminates human error and realizes labor-saving and efficient dissolution testing.

This article reports the results of an on-line dissolution test of loxoprofen sodium tablets using Nexera FV.

■ On-line dissolution testing with Nexera FV

A sampling device for dissolution tester and a filtration device are required to build up an on-line dissolution testing system. Test solution sampled from the dissolution tester is filtered by the filtration device and introduced directly into a flow vial (see Fig. 2) contained in the autosampler of Nexera FV. Analysis is started by injecting the test solution into the HPLC flow path, following the aspiration of it in the flow vial.

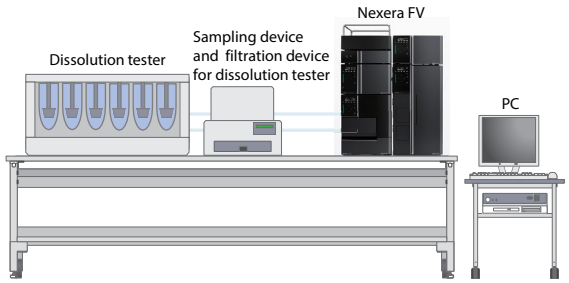


Fig.1 On-line dissolution test system setup using Nexera FV

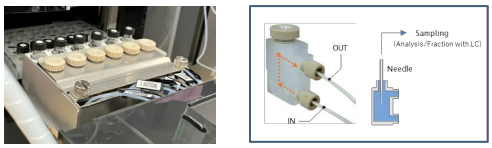


Fig.2 Flow vial

Nexera FV offers two different analysis modes: fraction analysis mode and direct injection analysis mode.

In fraction analysis mode, the test solution from the dissolution tester is once fractionated into vials or microtiter plate, and sampling intervals as short as 5 minutes can be supported. LC analyses can be performed collectively after the dissolution testing is completed or inserted between sampling intervals. An automatic dilution and an automatic addition of internal standard can be supported in this mode as well.

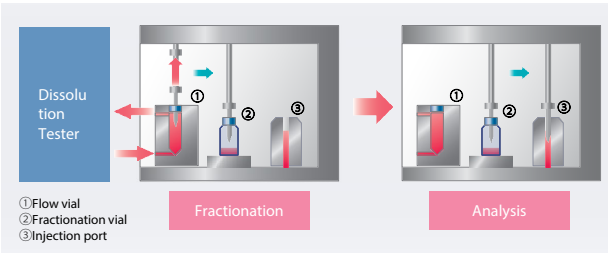


Fig.3 Fraction analysis mode

In direct injection analysis mode, the test solution from the dissolution tester is injected directly from a flow vial into the HPLC. After the test solution in first flow vial has been analyzed, the test solution in the second flow vial is subjected to HPLC analysis. This mode is useful when the sampling interval is large enough.

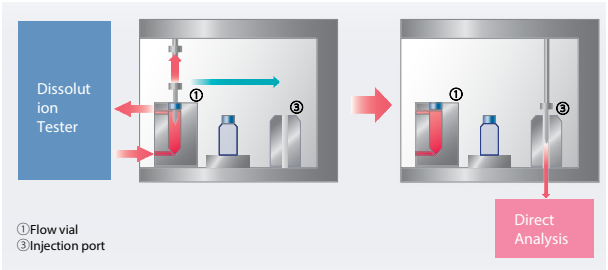


Fig.4 Direct injection analysis mode

■ On-line dissolution test of loxoprofen sodium tablets

On-line dissolution test of loxoprofen sodium tablets was performed. The HPLC conditions were optimized based on those described in the Japanese Pharmacopoeia 18th Edition as determination method for "Loxoprofen Sodium Tablets" to allow ultra high-speed analysis, which provides reductions of the retention time to 1 minute and the analysis time to 1.5 minutes. Table 1 shows the dissolution test conditions and Table 2 shows the HPLC analytical conditions.

Table 1 Dissolution test conditions

System	:	NTR-6600AST (TOYAMA SANGYO CO., LTD.)
Dissolution method	:	Paddle
Dissolution media		Water
Media volume	:	900 mL
Rotation speed	:	50 rpm
Bath temperature	:	37 ℃
Total time	:	30 min
Sampling time	:	5、10、15、20、25 and 30 min

Table 2 HPLC analytical conditions

Column	:	Shim-pack™ XR-ODS Ⅱ *1 (75 mm × 3.0 mm I.D., 2.2 µm)
Mobile phase	:	Methanol/Water/Acetic Acid/Triethylamine =600 : 400 : 1 : 1
Flow rate	:	0.8 mL/min
Column temp.	:	40 ℃
Injection vol.	:	2 µL
Detection	:	UV 222 nm

*1 P/N：228-41624-91

●Analysis of standard solution

Using a 1.5 mL ordinary vial, six repeated analyses of a standard solution of loxoprofen sodium (60 mg/L) were performed. Fig. 5 shows the chromatograms and Table 3 shows the results. Good results of around 0.05% RSD for both retention time and peak area values were obtained.

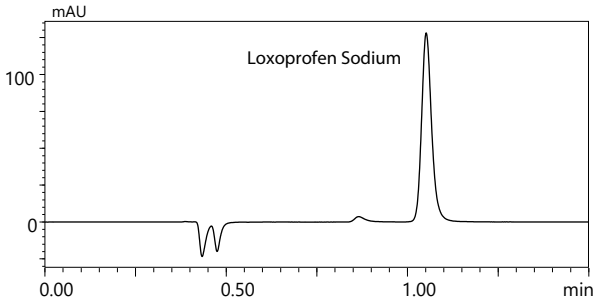


Fig.5 Chromatogram of standard solution of loxoprofen sodium (60 mg/L)

Table 3 Retention Time repeatability and peak area repeatability for a standard solution (60 mg/L、n=6)

	Retention time (min)	Area
1st	1.051	248,209
2nd	1.052	248,265
3rd	1.053	248,129
4th	1.052	248,232
5th	1.052	248,380
6th	1.051	248,038
Averages	1.052	248,209
%RSD	0.07	0.05

●Fraction analysis mode

The test solutions were sampled six times at 5, 10, 15, 20, 25, and 30 minutes. Fig. 6 shows the chromatogram of the test solution loxoprofen sodium tablet (68.1 mg per tablet indicated, dissolution time; 30 minutes).

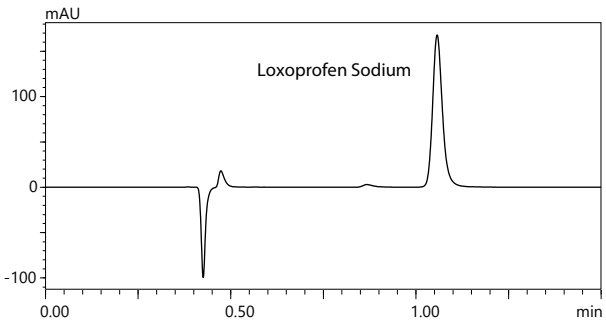


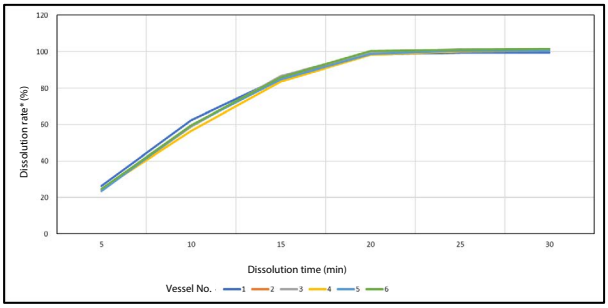
Fig.6 Chromatogram of test solution of loxoprofen sodium tablet (dissolution time; 30 min)

Table 4 shows the time-dependent variation of the dissolution rate in each vessel, and Fig. 7 shows the dissolution curve of loxoprofen sodium tablets.

The Japanese Pharmacopoeia, as ascribed, specifies that the dissolution rate of loxoprofen sodium tablets must be at least 85% in 30 minutes, and the results obtained from this study met this criterion.

Table 4 Time-dependent variation of dissolution rate in each vessel (%)

Time (min) / Vessel No.	5	10	15	20	25	30
1	26.28	62.34	85.67	98.45	99.53	99.49
2	23.88	59.71	84.98	99.07	101.08	100.89
3	23.90	58.78	86.68	99.80	101.27	101.18
4	24.33	56.44	83.55	98.18	100.25	100.64
5	23.54	59.62	84.81	98.77	100.54	100.61
6	24.77	59.54	85.97	100.41	101.15	101.59



*：Dissolution rate(%)=Concentration(mg/L)×Media Volume 0.9(L)/Labeled amount 68.1(mg)×100

Fig.7 Dissolution curves

●Direct injection analysis mode

Then, on-line dissolution test in direct injection analysis mode was performed. The test solutions from six vessels were sampled at 30 minutes only. Table 5 shows the dissolution rate in each vessel. In direct injection analysis mode, each dissolution rate 30 minutes was over 85%, which met the criterion as well.

Table 5 Dissolution rate (%) in each vessel

Time(min) / Vessel No.	30
1	103.49
2	101.67
3	100.40
4	100.29
5	102.42
6	102.32

■ Conclusion

In this article, an on-line dissolution test of loxoprofen sodium tablets using Nexera FV has been reported. The fraction analysis mode allows 5-minute sampling interval. The direct injection analysis mode doesn't require preparing vials for fractionation resulting in cost reduction. Thus, Nexera FV is an on-line HPLC system setup that can provide automated and efficient dissolution testing for drug products.

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