SHIMADZU
Excellence in Science

Application News

HPLC
High Performance Liquid Chromatography

No.LC-20-ADI-042

Online dissolution of Metformin ER tablets using Electrolab Veritas-08 with Shimadzu Nexera FV

Introduction

Extended release (ER) or sustained release dosage forms are designed to release a drug at predetermined rate in order to maintain a constant drug concentration for a specific period of time with minimum side effects. This can be achieved through variety of formulations.

Due to modified dosage forms, dissolution study to assess quality and absorption patterns must be checked over longer durations. This means the dissolution tests are in these cases generally run for more than 16 hours. Needless to say, this presents both technical and administrative challenges.

Maintaining complete traceability and avoiding errors are big tasks in hand for lab managers running ER dissolution assays.

Under these circumstances, it's highly desired to have an automated workflow starting from setting up of batch and aliquoting till reporting.

Such a set-up will also enable operations without the need of a chemist with complete reliability.

Most critical aspect and need of hour, irrespective of formulation type is ensuring compliance. An automated set-up with complete compliance is need of an hour so as to ensure higher productivity and reduced errors with full traceability.

KEYWORDS: Nexera FV, Veritas 8, online dissolution, compliance, Metformin dissolution reports.

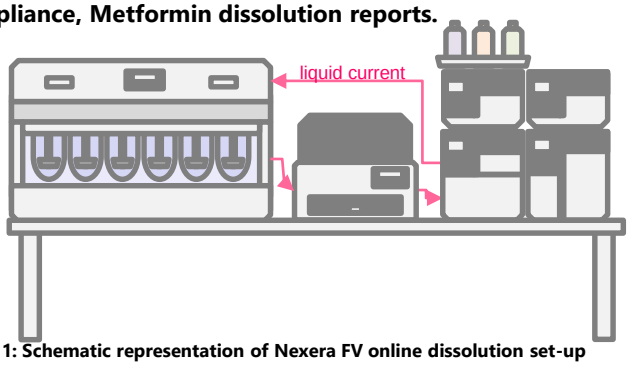


Figure 1: Schematic representation of Nexera FV online dissolution set-up

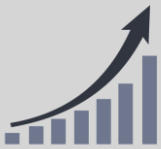
Shimadzu Nexera FV connected to Electrolab dissolution tester, enables automation of the entire dissolution testing process. Since complete workflow from dissolution to reporting is automated and monitored through a single platform of LabSolutions software, entire process has complete traceability and compliance.

Sequence of automatic sample aspiration with Nexera FV is as follows:
1. Displace flow vial with sample
2. Aspirate sample from flow vials
3. Analyze directly or fractionate into vials
4. Generate report

Key features

Compliance
- Direct sampling
- Audit trail and log for entire process- dissolution test parameters to sample processing and reporting
- Complete traceability of dissolution sample
- Direct reporting of dissolution result

High throughput
- Ideal even for profile with 5 min sampling intervals
- Walk away operation and analysis
- Fast analysis by UHPLC
- Reduction of errors- sampling and sample preparation error



Ease of use
- 3 stage online filtration
- Online dilution
- Quick reporting
- Retain samples in autosampler

Nexera FV provides a means for not only directly sampling the aliquots, but also dilution and HPLC analysis of the samples during the entire test duration for ER tablets resulting in completion of dissolution test and HPLC analysis simultaneously without human intervention.
Complete process from dissolution to reporting is automated and monitored through a single platform of LabSolutions Software, thus maintaining compliance.
Present work demonstrates the applicability of the Veritas-08 and Nexera FV online dissolution-HPLC system by performing automated dissolution analysis of metformin extended release tablets 1000mg as per USP monograph.

Method of analysis

Table 1: Dissolution and LC parameters

Dissolution parameters	
Apparatus	USP type II(Paddle)
Dissolution media	Phosphate buffer pH 6.8
Media volume	1000 mL
Bath temperature	37 °C
Rotational speed	100 rpm
Time	720 min
Time points	5, 10, 15, 20, 25, 30, 60, 120, 240, 360, 480, 600 and 720 min

LC parameters	
Column	Shiseido C18,4.6mm x150mm,5µm
Column temperature	45°C
Flow rate	0.75 mL/min
Injection volume	2 µL
Wavelength	218 nm
Detector cell temperature	45 °C
Autosampler temperature	4 °C
Mobile phase buffer	0.5 g/L sodium heptane sulfonate and 0.5g/L sodium chloride in water. Adjust pH to 3.85 with phosphoric acid.
Mobile phase	Acetonitrile:buffer (10:90)
Online dilution	10 times
Standard concentration	100 ppm

Result and discussion

An extended release formulation of metformin was tested for its dissolution profile at time points of 5, 10, 15, 20, 25, 30, 60, 120, 240, 360, 480, 600 and 720 min. Sampling was done in fractionation mode and autosampler dilution feature was used to avoid any manual intervention. Representative HPLC chromatogram are shown in Figure 2.

System suitability samples were assessed for percentage deviation of retention time and area, and results were found to be acceptable as shown in Table 2. Dissolution profile was found to be acceptable based on 80% release criteria (as shown in Figure 3). Percentage release value for 6 vessel for all 8 sampling points is tabulated in Table 3.

LabSolutions multi data report function was used for auto generation of report and dissolution profile. Not only automation but complete compliance is achieved using Veritas-08 and Nexera FV

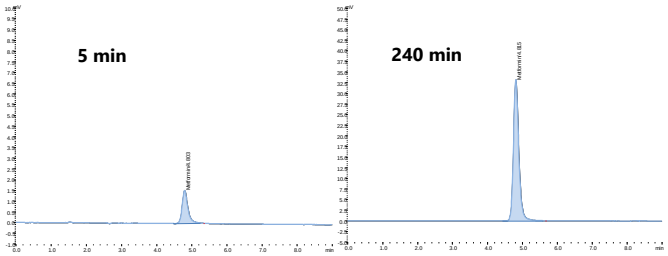


Figure 2. Representative chromatogram for Metformin (L) 5 min (R) 240 min

Table 2: System suitability results

Vessel	Quantitation standard		Bracketting standard	
	Area	RT	Area	RT
1	425470	4.793	446827	4.794
2	429197	4.792	448733	4.794
3	434201	4.796	448801	4.794
4	433579	4.796	449278	4.796
5	435073	4.795	450121	4.799
6	436181	4.794	448438	4.799
Max.	436181	4.796	450121	4.799
Min.	425470	4.792	446827	4.794
Average	432284	4.794	448700	4.796
Standard deviation	4105.7	0.002	1090.1	0.002
%RSD	0.950	0.037	0.243	0.05

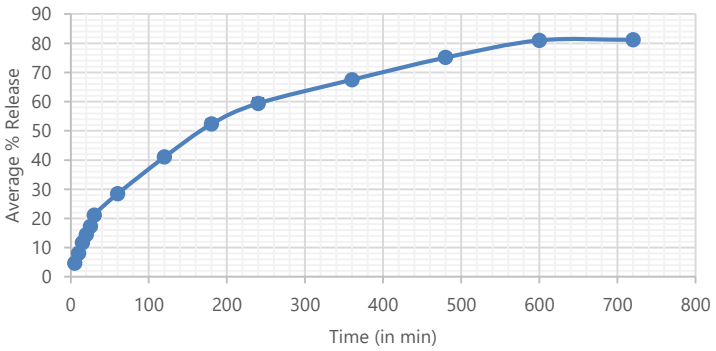


Figure 3. Dissolution profile for metformin extended release formulation

Table 3: Percentage release value for 6 vessels at different time points

		% Release													
Time (min)		5	10	15	20	25	30	60	120	180	240	360	480	600	720
Vessel No.	1	5.1	7.7	11.9	14.6	18.2	21.9	28.2	41.2	51.3	59.7	67.1	73.8	81.2	81.9
	2	4.5	8	11.8	13.2	17.3	20.7	27.5	38.2	51.7	56.2	66.5	73.2	80.7	80.7
	3	4.9	8.7	12.1	15.2	16.2	20.5	28.5	41.2	55.5	61.0	70.0	76.4	80.1	80.1
	4	4.9	8.8	11.9	14.1	17.1	19.8	29.1	41.9	51.8	59.5	66.7	75.1	82.4	82.4
	5	5.0	8.0	12.0	14.3	16.9	22.0	27.1	41.5	52.3	59.0	67.5	76.3	79.6	79.9
	6	3.8	7.5	10.2	14.9	18.0	21.6	30.1	41.8	51.4	61.2	67.0	75.9	82.1	82.1
Max.		5.1	8.8	12.1	15.2	18.2	22	30.1	41.9	55.5	61.2	70.0	76.4	82.4	82.4
Min.		3.8	7.5	10.2	13.2	16.2	19.8	27.1	38.2	51.3	56.2	66.5	73.2	79.6	79.9
Average		4.7	8.1	11.7	14.4	17.3	21.1	28.4	41.0	52.3	59.4	67.5	75.1	81.0	81.2
Standard deviation		0.5	0.5	0.7	0.7	0.7	0.9	1.1	1.4	1.6	1.8	1.3	1.3	1.1	1.1
%RSD		10.3	6.4	6.1	4.8	4.2	4.1	3.8	3.3	3.0	3.0	1.9	1.7	1.3	1.3

SHIMADZU
Excellence in Science

Shimadzu Analytical (India) Pvt.Ltd.
1 A/B, Rushabh Chambers, Makwana Road,
Marol, Andheri (East), Mumbai- 400059, India.
Tel: +91 22 29204741 Fax: +91 22 29205679
www.shimadzu.in

Related Products Some products may be updated to newer models.

Nexera FV

Ultra High Performance Liquid Chromatograph for On···

Related Solutions

Life Science

Price Inquiry

Product Inquiry

Technical Service / Support Inquiry

Other Inquiry