SHIMADZU
Excellence in Science

Application News

No. L523

High Performance Liquid Chromatography

Analysis of Irbesartan Using an Integrated LC System - Nexera™-i MT

Ultra-high performance liquid chromatographs (UHPLC) are becoming more common in recent years and there will likely be more cases where UHPLC analytical conditions are specified in pharmacopoeias. On the other hand, however, the popularity of UHPLCs is still small in the manufacturing sector for quality control department and makes up only 9 % of the total UHPLC market in contrast to the R&D sector's 38 %.[1] For this reason, applying the analytical conditions specified in the pharmacopoeias may not be adequate for quality control department.

Irbesartan and amlodipine besilate tablets[2] are newly listed in Supplement 1 to the 17th Edition of the Japanese Pharmacopoeia (JP), which specifies a column packing particle size of 2.2 µm meaning that a UHPLC needs to be used. Due to the pressure tolerance of the instrument, applying the analytical conditions may not be possible as described.

Under such circumstances, Notification No. 0331-1, issued by the Director of the Evaluation and Licensing Division, Pharmaceutical Safety and Environmental Health Bureau, MHLW, states that, on the understanding that the monograph of the drug being tested shall be revised, an application for approval of such drugs is possible by employing analytical conditions using conventional liquid chromatography on the basis of appropriate analytical validation data. The notification is considered to be indicating that it is acceptable to change the JP listed conditions to conventional (HPLC) conditions.

This article introduces a system suitability test and analysis using the listed conditions transferred to an HPLC conditions for quantitative determination of irbesartan in irbesartan and amlodipine besilate tablets that are newly listed in Supplement 1 to the 17th Edition of the JP, using a Shimadzu integrated LC system, Nexera™-i MT.

Y. Osaka

System Suitability Test

Table 1 shows the analytical conditions used for a system suitability test in the quantitative determination of irbesartan and amlodipine besilate tablets. Fig. 1 shows the obtained chromatograms. In addition, Table 2 shows the results of the system suitability test, indicating that the system has passed the criteria of the test.

Table 1 Analytical Conditions for Quantitative Determination of Irbesartan and Amlodipine Besilate Tablets

Column	: Shim-pack™ XR-ODSII 75 mmL. × 3.0 mmI.D., 2.2 µm
Mobile phase	: Methanol / 0.02 mmol/L (Sodium) Phosphate Buffer (pH3.0) = 3 / 2
Flow rate	: 0.8 mL/min
Column temp.	: 40 °C
Injection volume	: 5 µL
Detection	: UV 237 nm (Semimicro Cell)
Sample	: Irbesartan and Amlodipine Besilate

Table 2 Results of System Suitability Test

Test Item	Criteria	Result	Judgement
Resolution (between Amlodipine Besilate and Irbesartan)	≥ 5	14.50	PASSED
Relative standard deviation of Area (N = 6)	≤ 1.0 %	0.145	PASSED

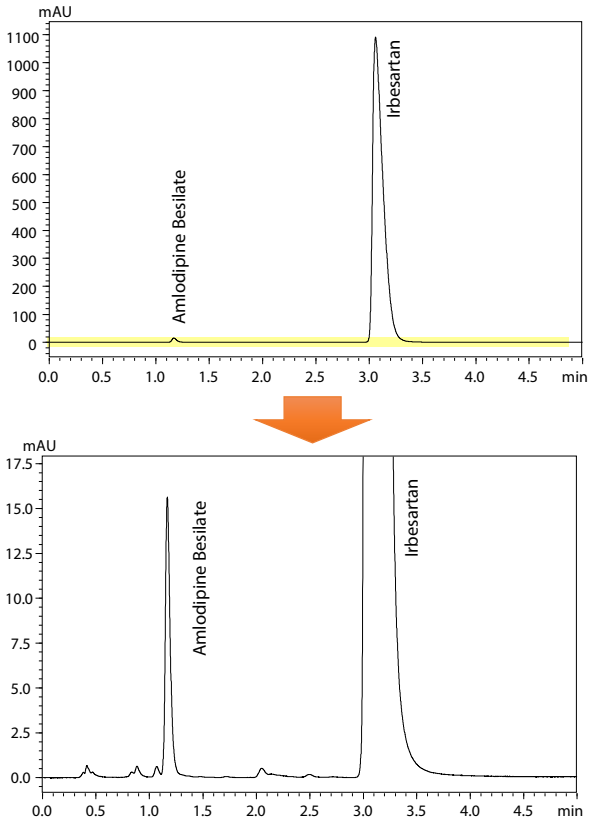

Fig. 1 Results of Irbesartan (and Amlodipine Besilate) Analysis

Transfer to HPLC Analytical Conditions

Nexera-i MT has two independent flow paths of HPLC and UHPLC in a single instrument. Since a suitable column can be set for each path, there is no need to change the column when transferring the method from UHPLC to HPLC.

As of January 2018, the allowable adjustment range of listed analytical conditions that does not need revalidation is not specified in the JP. However, the JP, US Pharmacopoeia (USP) and European Pharmacopoeia (EP) are aiming for international harmonization to attempt unifying the allowable adjustment range of analytical conditions. In this experiment, we changed the analytical conditions based on the public comments on the proposal for international harmonization issued in July 2017.[3] Note that the range in the proposal for international harmonization may not be the same as that adopted finally.

Allowable Adjustment Range for Isocratic Elution

In the proposal for international harmonization, the allowable adjustment range of isocratic elution is described in detail.[3] Some major points are introduced below.

Column dimensions: The ratio of the column length (*L*) to the particle size (*dp*) *L/dp* must be in the range of −25 to +50 %. Ratios are defined separately for columns packed with superficially porous particles.

Flow rate: When the particle size is changed, the flow rate may require adjustment. Use the following equation.

$F_2 = F_1 \times [(dc_2^2 \times dp_1) / (dc_1^2 \times dp_2)]$ … (A)

F_1 : Flow rate indicated in the monograph (mL/min)

F_2 : Adjusted flow rate (mL/min)

dc_1 : Internal diameter of the column indicated in the monograph (mm)

dc_2 : Internal diameter of the column used (mm)

dp_1 : Particle size of the column indicated in the monograph (µm)

dp_2 : Particle size of the column used (µm)

In addition, when a change is made in particle size from less than 3 µm to 3 µm or more, an additional reduction of linear velocity (flow rate) may be required to avoid reduction in column efficiency by more than 20 %. After an adjustment due to a change in column dimensions, an additional change in flow rate of ±50 % is permitted.

Based on the above, the method used for quantitative determination of irbesartan and amlodipine besilate tablets is transferred to an HPLC analytical condition. The adjustments are listed in Table 3.

Table 3 Adjustments to Analytical Conditions Allowable by the Proposal for International Harmonization

	Based on JP	Transfer (HPLC)	Note
Column length (*L*) (mm)	75	150	User choice
Column diameter (*dc*) (mm)	3.0	4.6	User choice
Particle size (*dp*) (µm)	2.2	5.0	User choice
L/dp	34.1	30.0	−12 %
Flow rate (mL/min)	0.8	1.0	*1

*1 The solution of formula (A) is approx. 0.83 mL/min. Since a change of ±50 % is allowed, 1.0 mL/min was used.

Results of HPLC Analysis

Table 4 shows the detailed analytical conditions. The obtained chromatograms are shown in Fig. 2, and the results of the system suitability test according to the JP are shown in Table 5. At the time of this writing, although this method cannot be accepted without revalidation, we confirmed that the obtained results satisfied the criteria of the system suitability test required by the JP.

Table 4 HPLC Analytical Conditions

Column	: Shim-pack™ VP-ODS 150 mmL. × 4.6 mmI.D., 5.0 µm
Mobile phase	: Methanol / 0.02 mmol/L (Sodium) Phosphate Buffer (pH3.0) = 3 / 2
Flow rate	: 1.0 mL/min
Column temp.	: 40 °C
Injection volume	: 10 µL
Detection	: UV 237 nm (Semimicro Cell)
Sample	: Irbesartan and Amlodipine

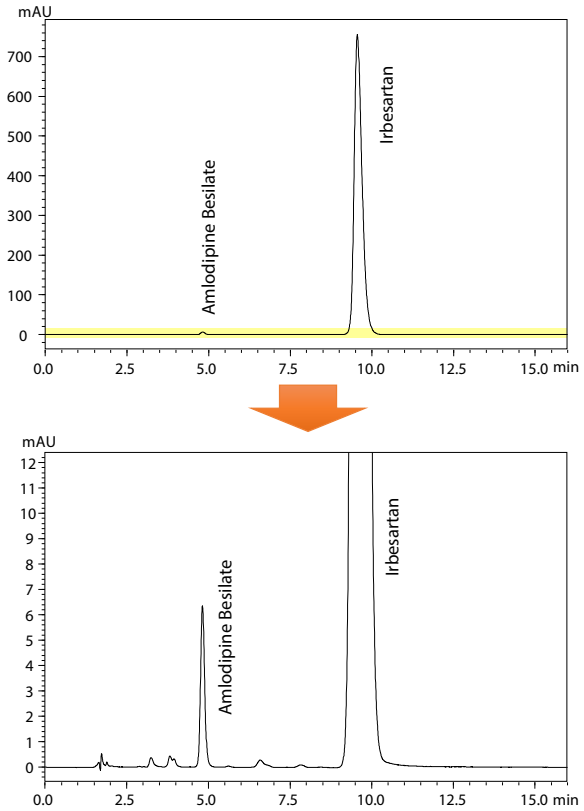

Fig. 2 Results of Irbesartan (and Amlodipine Besilate) HPLC Analysis

Table 5 Results of System Suitability Test

Test Item	Criteria	Result	Judgement
Resolution (between Amlodipine Besilate and Irbesartan)	≥ 5	13.9	PASSED
Relative standard deviation of Area (N = 6)	≤ 1.0 %	0.212	PASSED

<References>
(1) Strategic Directions International, Inc. Ultra-High Performance Liquid Chromatography (UHPLC) Published May 2016
(2) Supplement 1 to the 17th Edition of the Japanese Pharmacopoeia (JP), 42-44
(3) Proposal for International Harmonization (Stage 4), Pharmaceuticals and Medical Devices Agency (http://www.pmda.go.jp/rs-std-jp/standards-development/jp/pub-comments/pdg/0033.html)

First Edition: Jul. 2018

Shimadzu Corporation
www.shimadzu.com/an/

Related Products Some products may be updated to newer models.

Shim-pack XR Series
HPLC Column

Shim-pack VP Series
HPLC Column

Related Solutions

Price Inquiry

Product Inquiry

Technical Service / Support Inquiry

Other Inquiry