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USP Method Transfer and Routine Use Analysis of Irbesartan Tablets from HPLC to UPLC

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APPLICATION BENEFITS

- 85% reduction in run time
- 91% reduction in solvent consumption
- 86% reduction in sample consumption
- Columns available in both UPLC® and HPLC particle sizes
- Proven column performance of over 3000 injections on the ACQUITY UPLC® column for Irbesartan tablets

WATERS SOLUTIONS

Alliance® HPLC system

ACQUITY UPLC® system

ACQUITY UPLC HSS T3 and XSelect™ HSS T3 columns

Method Transfer kits

Empower™ 2 CDS software

Waters Irbesartan standard

KEY WORDS

ACQUITY UPLC Columns Calculator, Waters Reversed-Phase Column Selectivity Chart, method transfer, USP, irbesartan, tablets, UPLC, HSS, routine use

INTRODUCTION

While it is advantageous to transfer compendial methods that do not take advantage of recent advancements in chromatographic chemistries and instrumentation to UPLC technology, these migrated methods are only valuable when they are robust enough for routine use.

In this study we use the USP monograph for irbesartan as an example to transfer the long HPLC run to a short UPLC run. Irbesartan is marketed as AVAPRO® through a partnership between Bristol-Myers Squibb Company and Sanofi-Aventis. AVAPRO ($1.18B sales in FY 2010) is prescribed for treatment of high blood pressure and diabetic nephropathy. The drug's patent is expected to expire in 2012. Several companies may begin manufacturing a generic AVAPRO drug once it goes off-patent.

A routine use study of over 3000 injections is shown by ensuring proper handling of the irbesartan tablet sample preparation and effectively managing chromatographic variables such as operating conditions delivered by the instrument. Following the process described here will help with the successful adoption of modern UPLC technology and its benefits to test products described in the Pharmacopeial monographs.

EXPERIMENTAL

HPLC Conditions

LC System:	Alliance® HPLC with 2489 UV/Visible detector
Run Time:	20 minutes
Column:	XSelect™ HSS T3, 4.6 x 250 mm, 5 µm (USP designation: L1), part number 186004793
Mobile Phase:	Acetonitrile and buffer solution (40:60); buffer solution: 0.55% phosphoric acid in water adjusted to pH 3.0 with triethylamine
Wash Solvent:	70/30 water/acetonitrile
Separation Mode:	Isocratic
Flow Rate:	1.0 mL/min
Injection Volume:	10 µL
Detection:	UV at 220 nm
Temperature:	30 °C

UPLC Conditions

LC System:	ACQUITY UPLC with TUV detector
Run Time:	3 minutes
Column:	ACQUITY UPLC HSS T3 2.1 x 100 mm, 1.8 µm (USP designation: L1), part number 186003539
Mobile Phase:	Acetonitrile and buffer solution (40:60); buffer solution: 0.55% phosphoric acid in water adjusted to pH 3.0 with triethylamine

RESULTS AND DISCUSSION

The USP monograph for irbesartan requires the use of a YMC™ ODS-A 4.6 x 250 mm, packing (L1) column.[1] The Waters Reversed-Phase Column Selectivity Chart recommends that the equivalent Waters column is XSelect HSS T3. The chromatograms for the irbesartan standard and tablet sample analysis using the XSelect HSS T3 4.6 x 250 mm, 5 µm, (L1) column on an Alliance HPLC system are shown in Figure 1.

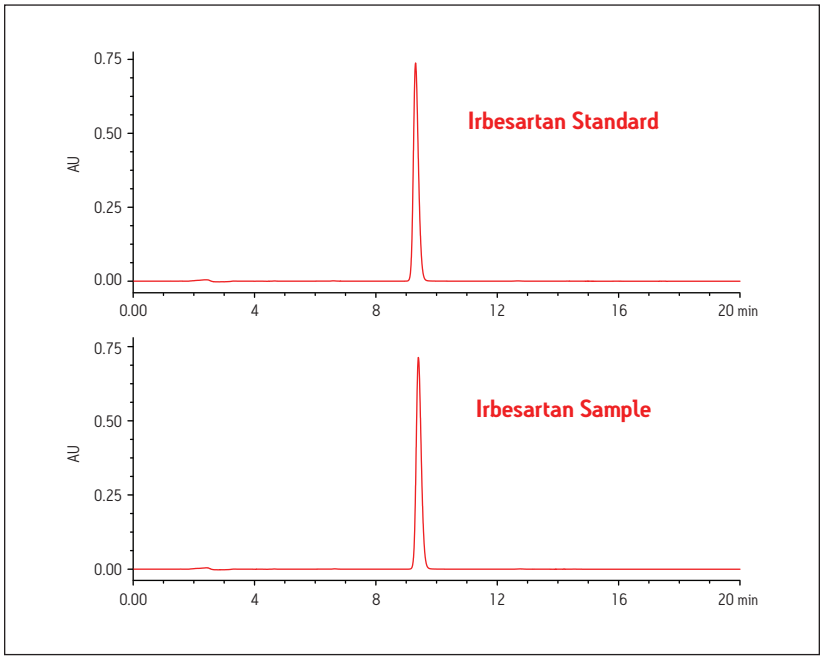

Figure 1. USP irbesartan standard and tablet sample run on an XSelect HSS T3 4.6 x 250 mm, 5 µm column on the Alliance HPLC system.

The USP method was then transferred from HPLC to UPLC using the Waters ACQUITY UPLC Columns Calculator as described in the application note "Implementation of Methods Translation between Liquid Chromatography Instrumentation", part number 720003721en.[3] The retention factor (*k'*) of irbesartan, calculated from the separation on Alliance, was input into the columns calculator to optimally scale the method and generate UPLC method conditions while preserving the resolving power of the separation. The separation of irbesartan standard and sample injected on the ACQUITY UPLC system configured with the Waters ACQUITY UPLC HSS T3 2.1 x 100 mm, 1.8 µm, (L1) column is shown in Figure 2.

Wash Solvents:	70/30 water/acetonitrile (600 µL of weak wash) 100% acetonitrile (200 µL of strong wash)
Separation Mode:	Isocratic
Flow Rate:	0.58 mL/min
Injection Volume:	1.4 µL
Detection:	UV at 220 nm
Temperature:	30 °C
Data Management:	Empower 2 CDS

USP System Suitability Criteria

% Area RSD ≤ 1.5 for 5 replicate injections

Standard preparation

An accurately weighed quantity of irbesartan was dissolved in methanol to obtain a stock solution of 15 mg/mL. This stock solution was diluted 100-fold in methanol to obtain a working solution of 0.15 mg/mL as required by the USP assay method guidelines in USP Monograph for Irbesartan: USP34-NF29.

Sample preparation

The concentration of the working standard and sample specified in the USP monograph is 0.15 mg/mL.[1] The sample was prepared from AVAPRO (irbesartan) tablets as specified in the USP Monograph for Irbesartan: USP34-NF29. Five tablets of irbesartan were weighed and finely powdered. An equivalent of 15 mg of this powder was weighed and transferred to a 100-mL volumetric flask. 75 mL of methanol was added to the flask and this solution was sonicated for 15 minutes, with stirring at 5-minute intervals. Methanol was added to make up the volume to 100 mL and this solution was passed through a 0.45-µm porous glass microfiber membrane filter.[1]

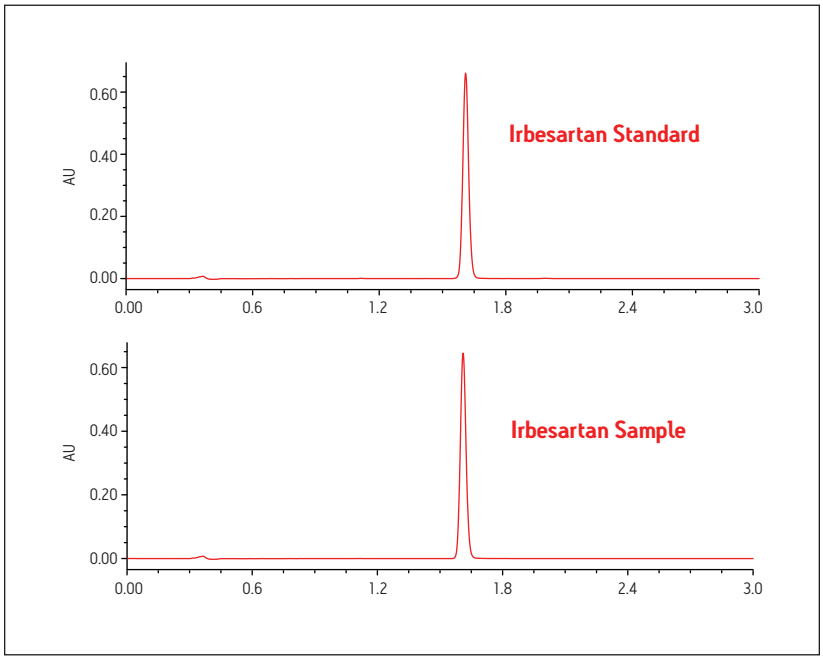

Figure 2. USP irbesartan standard and tablet sample run on a 2.1 x 100 mm ACQUITY UPLC HSS T3 column on an ACQUITY UPLC system.

System suitability requirements for the irbesartan separation on the Alliance HPLC system and the ACQUITY UPLC system were met (Table 1).

USP Requirements	Irbesartan Standard (HPLC)	Irbesartan Tablet (HPLC)	Irbesartan Standard (UPLC)	Irbesartan Tablet (UPLC)
% Area RSD ≤ 1.5 (n=5)	0.31	0.12	0.30	0.30

Table 1. System suitability results for five replicate injections of irbesartan standard and tablet sample for transfer of USP method from the Alliance HPLC to the ACQUITY UPLC system.

ROUTINE USE STUDY

Once the method was successfully transferred from HPLC to UPLC with the system suitability parameters meeting the assay requirements, a routine use study was initiated on the UPLC system. Following the protocol that a typical QC lab would use to perform the USP monograph testing, a sample set was constructed with two replicate injections of standard bracketing 6 replicate injections of sample.

The method reliability and performance was monitored during the routine use study by assessing the area %RSD for five replicate injections. The system suitability criterion for the five replicate injections was required to be less than or equal to 1.5% throughout periodic system checks during the experimental evaluation. System pressure was also monitored throughout the course of the study as a second indicator of method performance and reliability. As shown in Table 2, the %RSD for Irbesartan peak area for 5 replicate injections was well within the USP specifications throughout the course of the study. System pressure also remained stable at around 10,800 psi for approximately 3000 injections (Figure 3).

Injection #/ System Suitability Requirements	21 – 25	613 – 617	1325 – 1329	1919 – 1923	2513 – 2517	2985 – 2989
% Area RSD ≤ 1.5	0.30	0.15	0.41	0.44	0.17	0.43

Table 2. System suitability results for routine use evaluation of over 3000 injections on the ACQUITY UPLC HSS T3 column used on an ACQUITY UPLC system.

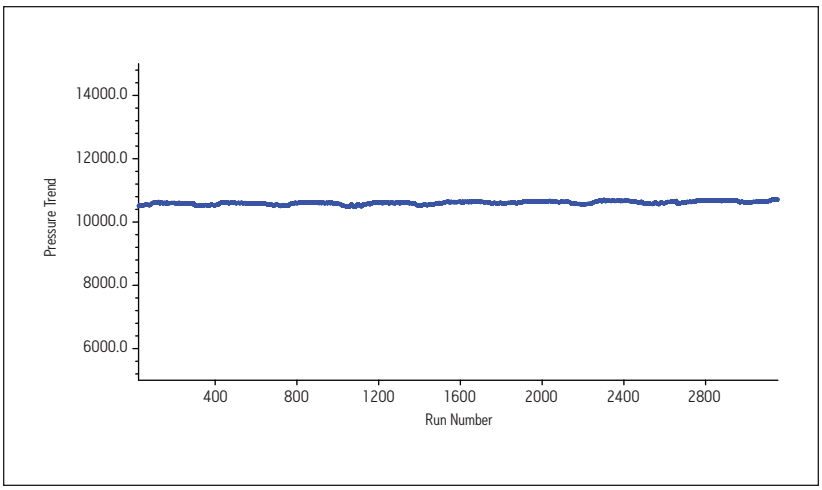

Figure 3. System pressure trend plot from routine use evaluation of over 3,000 injections on the ACQUITY UPLC HSS T3 column.

CONCLUSIONS

USP method for irbesartan, USP Monograph USP34-NF29, was successfully transferred from the original HPLC method to the UPLC platform running modern sub-2 µm column chemistry. The transfer was facilitated by use of the ACQUITY UPLC Columns Calculator and the Waters Reversed-Phase Column Selectivity Chart. System suitability requirements for the USP method transferred from the Alliance HPLC system to the ACQUITY UPLC system were met. The ACQUITY UPLC HSS T3, 1.8 µm column demonstrated robust and reliable performance at low pH (3.2) conditions for over 3000 injections. Other benefits realized by transferring this methodology were an 85% reduction in run time, 91% reduction in solvent consumption and 86% reduction in sample consumption. The ease of transfer using the simplistic workflow design[3] helps in the seamless adoption of UPLC technology with conspicuous gains in overall laboratory efficiency and productivity for running USP monographs.

References

1. USP Monograph. Irbesartan, USP34-NF29, 3187. The United States Pharmacopeial Convention, official from May 1, 2011.
2. USP Chapter 621. USP34-NF29, 243. *Pharmacopeial Forum* **35**(6): 1516.
3. Jones M.D., Alden P., Fountain K.J., Aubin A. *"Implementation of Methods Translation between Liquid Chromatography Instrumentation,"* Waters Application Note [2010]; Part Number 720003721EN.

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