[TECHNOLOGY BRIEF]

HPLC Method Transfer for Analysis of Metoclopramide HCl and Related Substances from an Agilent 1100 Series LC System to an ACQUITY Arc System

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GOAL

To transfer an HPLC method for related substances of metoclopramide HCl from an Agilent 1100 Series LC System to an ACQUITY® Arc™ System, replicating the chromatographic separation and meeting system suitability specifications.

BACKGROUND

Analytical methods used for testing of pharmaceutical raw materials and finished products are often transferred across organizations or to contract partners that utilize instruments from different vendors. It is therefore essential for the analytical laboratories to successfully transfer these methods, to ensure product consistency and compliance with regulations. Effective method transfer generates equivalent results for the same analysis, independent of the instrument, laboratory, or the resources. This is important to eliminate the need to revalidate the method, which is time consuming and costly.

Here, we present a transfer of the HPLC method for related substances analysis of metoclopramide HCl from an Agilent 1100 Series LC System to an ACQUITY Arc System. The success of the method transfer to the new instrumentation will be measured by examining the chromatographic separation for comparable results, and verifying that the system suitability results meet the specifications defined in the USP General Chapter <621> Chromatography.[1]

The ACQUITY Arc System successfully reproduced chromatographic separation obtained on the Agilent 1100 Series LC System, generating reliable, robust, and accurate results.

Compound	Common name
API	Metoclopramide HCl
Impurity A	4-Acetamido-5-chloro-N-(2-(diethylamino) ethyl)-2-methoxybenzamide
Impurity B	Methyl 4-acetamido-5-chloro-2-methoxybenzoate
Impurity C	4-Amino-5-chloro-2-methoxybenzoic acid
Impurity D	Methyl 4-acetamido-2-methoxybenzoate
Impurity F	4-Amino-5-chloro-N-(2-(diethylamino) ethyl)-2-hydroxybenzamide
Impurity G	2-(4-Amino-5-chloro-2-hydroxybenzamido)-N, N-diethylethanamide oxide
Impurity H	4-Acetamido-2-hydroxybenzoic acid
Impurity 9	Methyl 4-amino-2-methoxybenzoate

Table 1. List of the USP specified related substances of metoclopramide HCl for method transfer.

THE SOLUTION

The related compounds of metoclopramide HCl used in this study are listed in Table 1. Separate stock solutions were prepared in methanol at 1.0 mg/mL. A metoclopramide stock solution was diluted with water to 0.5 mg/mL and spiked with related substances at 1.0% level. For a system suitability solution, each stock solution was transferred to one vial and diluted with water to 0.05 mg/mL concentration of each analyte. The mixture was then diluted with standard diluent (50:50 methanol/water) to 15 µg/mL concentration for system suitability determination.

The HPLC method was first run on an Agilent 1100 Series LC System and then transferred to an ACQUITY Arc System. The ACQUITY Arc System offers a novel Multi-flow path™ technology, which enables efficient method transfer of legacy methods developed on previous generations of LC instrumentation. Instrument conditions for transfer of the HPLC method are listed in Figure 1.

The chromatographic data of a sample containing metaclopramide API at 0.5 mg/mL with 1.0% of related substance acquired on both the Agilent 1100 Series LC and ACQUITY Arc Systems is displayed in Figure 2. The data shows that the ACQUITY Arc System reproduced chromatographic separation acquired on the Agilent 1100 Series LC System.

The mass spectral data acquired using an ACQUITY QDa® Detector coupled to an ACQUITY Arc System was used to confirm identity of metoclopramide and related substances by mass detection. The mass analysis window from Empower® 3 Software (Figure 3) shows UV and mass spectral data from a single result. This UV detection enhanced with MS spectral data was used to quickly confirm identity of the sample components.

Performance of the HPLC method on the ACQUITY Arc System was verified by evaluating system suitability of five replicate injections of the system suitability solution according to the requirements defined in the USP General Chapter <621> Chromatography[1] and compared to the results obtained on the Agilent 1100 Series LC System. Results of the method system suitability acquired on both systems passed the USP specifications and are summarized in Table 2. The retention times and peak areas repeatability of the method run on the ACQUITY Arc System were substantially lower than the USP specifications of less than 2.0% RSD and comparable to the Agilent 1100 Series LC System. The USP resolution values between all the peaks were comparable on both systems, indicating no loss in resolution for method transfer. The USP peak tailing factors were also comparable.

Parameter	Description
LC systems	**Agilent 1100 Series LC System** with quaternary pump and DAD detector **ACQUITY Arc System with 2998 PDA and ACQUITY QDa detectors**, passive pre-heater, and flow path 1
Column	XSelect™ CSH C_{18}, 4.6 x 150 mm, 5 µm
Column temp.	45 °C
Flow rate	2.9 mL/min
Injection volume	10.0 µL
Mobile phase	A: 0.1% formic acid in water B: 0.1% formic acid in methanol
Gradient	1 Initial 2.900 95.0 5.0 0.0 2 15.00 2.900 40.0 60.0 0.0 3 16.50 2.900 40.0 60.0 0.0 4 16.80 2.900 95.0 5.0 0.0 5 21.00 2.900 95.0 5.0 0.0
Wash solvents	Purge: 50:50 water/methanol Sample wash: 50:50 water/methanol Seal wash: 90:10 water/acetonitrile
PDA detection	λ range: 210 – 400 nm, Derived at 270 nm Sampling rate: 20 pts/sec
Mass detection	ACQUITY QDa Detector (ACQUITY Arc System only) Ionization mode: ESI+, ESI- Acquisition range: 100 – 440 *m/z*

Figure 1. Instrument conditions for transfer of the HPLC method for metoclopramide HCl and its USP-related substances from an Agilent 1100 Series LC System to an ACQUITY Arc System.

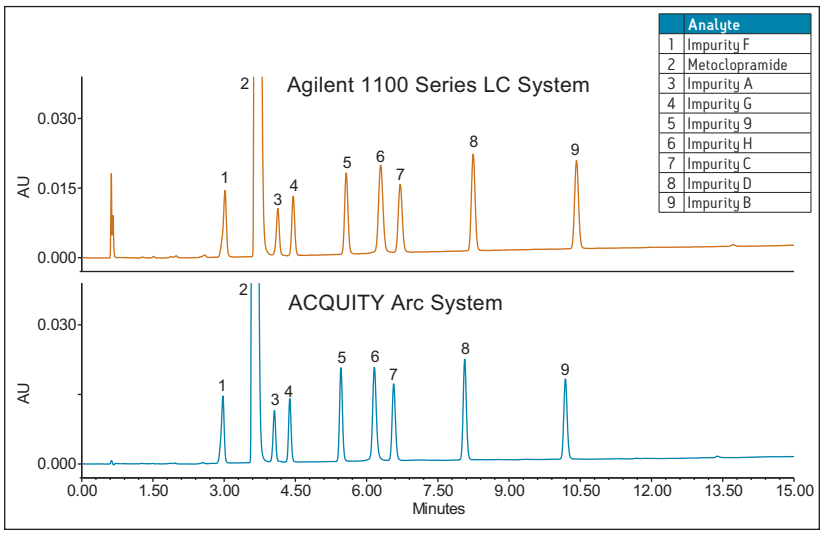

Figure 2. Chromatographic data of the metoclopramide API at 0.5 mg/mL with 1.0% of related substances for the method transfer from an Agilent 1100 Series LC System to an ACQUITY Arc System.

Compound	%RSD of retention time		%RSD of peak areas		USP resolution		USP peak tailing	
	Agilent 1100	ACQUITY Arc	Agilent 1100	ACQUITY Arc	Agilent 1100	ACQUITY Arc	Agilent 1100	ACQUITY Arc
Impurity F	0.02	0.09	0.26	0.04	n/a	n/a	0.8	0.9
API	0.01	0.05	0.28	0.10	6.1	6.5	1.0	1.1
Impurity A	0.02	0.04	0.32	0.02	3.3	3.6	0.9	1.0
Impurity G	0.02	0.03	0.35	0.13	2.8	3.3	1.1	1.1
Impurity 9	0.01	0.03	0.45	0.18	9.1	10.3	1.1	1.1
Impurity H	0.01	0.03	0.31	0.20	4.8	5.6	1.1	1.1
Impurity C	0.01	0.02	0.34	0.36	2.5	3.1	1.1	1.1
Impurity D	0.01	0.04	0.31	0.16	10.1	11.8	1.1	1.1
Impurity B	0.01	0.03	0.66	0.22	14.3	16.5	1.1	1.1

Table 2. System suitability results of five replicate injection of the system suitability solution for method transfer between Agilent 1100 Series LC and ACQUITY Arc systems.

Enabled by a unique Multi-flow path technology, the ACQUITY Arc System easily accepts and replicates methods from a variety of platforms, without compromising method integrity.[2] The ACQUITY Arc System provides powerful LC performance and secures the lab's investment by ensuring integration with new technologies such as the ACQUITY QDa Detector and the Empower Chromatography Data System (CDS) Software.

SUMMARY

The HPLC method for metoclopramide and its related substances was successfully transferred from an Agilent 1100 Series LC System to an ACQUITY Arc System. The ACQUITY Arc System successfully replicated the quality of chromatographic separation obtained on the Agilent 1100 Series LC System and met the USP specifications for system suitability. Meeting the system suitability requirements is essential for laboratories to remain in compliance with the current Good Laboratory Practices regulations. Moreover, the ACQUITY QDa Detector

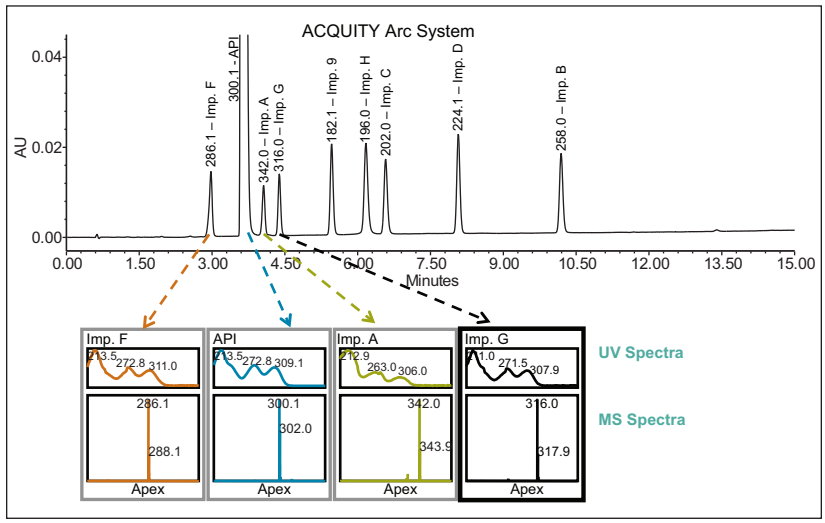

Figure 3. Confirming peak identity by mass detection using mass spectral data acquired with an ACQUITY QDa Detector. Mass analysis window from Empower 3 Software shows UV and mass spectral data from a single result.

in conjunction with UV detection enabled quick confirmation of peak identity by mass detection. Overall, the ACQUITY Arc System delivers reliable, robust, and reproducible results, which are key elements to enhance throughput and laboratory efficiency for routine testing in the QC laboratory.

References

1. USP General Chapter, <621> Chromatography, USP 37-NF 32, The United States Pharmacopeia Convention, Official December 1, 2014.

2. ACQUITY Arc System, http://www.waters.com/waters/nav.htm?cid=134844390

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