Time-Saving of Esomeprazole Magnesium Analysis -International Harmonization of Pharmacopoeia-

U200917AE

Ultra-high performance liquid chromatography (UHPLC) offers high throughput analysis and cost savings, such as analysis time and solvent consumption, and is widely used in the pharmaceutical industry. According to pharmacopoeias, many drugs are prescribed to be analyzed by high pressure liquid chromatography (HPLC) using conventional column dimensions and parameters. The United States Pharmacopeia (USP) and the International Harmonization of Pharmacopoeias allow for changes in LC parameters to the extent that they fulfill system suitability requirements for UHPLC. Based on the International Harmonization of Pharmacopoeias, the time-saving advantages of using UHPLC for the USP analysis for Esomeprazole Magnesium [ORGANIC IMPURITIES] is shown here.

Permissible Adjustment to LC Parameters under Isocratic Elution Conditions in International Harmonization of Pharmacopoeias

According to International Harmonization of Pharmacopoeias (Stage 4), the permissible adjustment to LC parameters under isocratic elution conditions is shown below.

【Column】

Stationary phase	Unchangeable
Particle size (dp)	L/dp is changeable in the range of −25% to +50%
Column length (L)	

【Mobile phase】

pH	±0.2
Salt concentration of buffer solution	±10%
Solvent composition	The minor solvent composition is changeable in the greater of ±30% (relative) or ±2% (absolute).

【Other LC parameters】

Flow rate	$F_2 = F_1 \times [(dc_2^2 \times dp_1)/(dc_1^2 \times dp_2)]$ F_1: original frow rate　F_2: modified flow rate dc_1: original column inner diameter　dc_2: modified column inner diameter dp_1: original particle size　dp_2: modified particle size When the particle sizes are changed from ≥ 3 µm to < 3 µm, F_2 is changeable within the range of ±50% if the column efficiency does not decrease by more than 20%.
Temperature	±10℃
Detector wavelength	Unchangeable
Injection volume	If the column dimension is changed, the injection volume is changeable according to the below equation. $V_{inj2} = V_{inj1} \times [(L_2 \times dc_2^2)/(L_1 \times dc_1^2)]$ V_{inj1}: original injection volume　V_{inj2}: modified injection volume L_1: original column length　L_2: modified column length dc_1: original column inner diameter　dc_2: modified column inner diameter Even if the column dimension is not changed, the injection volume is changeable within the range fulfilling the system suitability requirements.

*Please refer to the original article written by the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH).

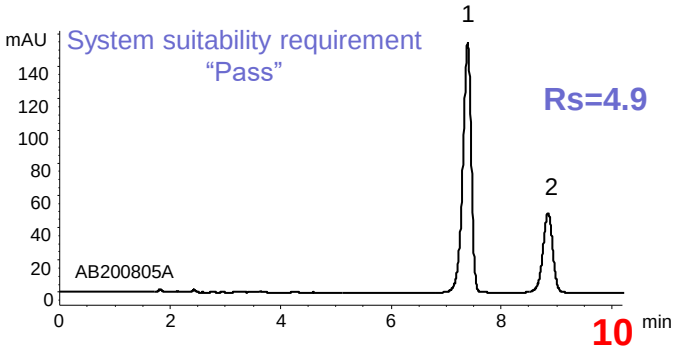
Time-Saving of the USP Analysis for Esomeprazole Magnesium

The LC analyses for Esomeprazole Magnesium [ORGANIC IMPURITIES], listed in USP 42, were performed under the USP-compliant and time-saving conditions. YMC-Triart C8, organic/inorganic hybrid silica based column categorized as packing L7, with particle size of 5 µm and column dimensions of 150 X 4.6 mm I.D. was used in the USP-compliant condition, while the time-saving analyses were performed with particle size of 3 µm and 1.9 µm with the permissible range of L/dp (22,500 ≤ L/dp ≤ 45,000).

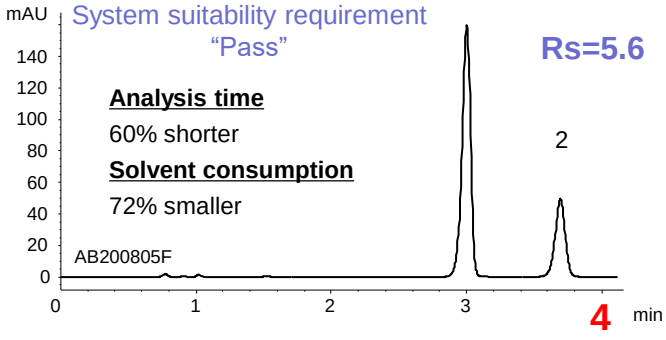
	USP Monograph	USP-compliant	Time-saving (HPLC)	Time-saving (UHPLC)
Column	5 µm packing L7, 125 X 4.0 or 150 X 4.6 mmI.D.	YMC-Triart C8, 5 µm, 150 X 4.6 mmI.D. (L/dp = 30,000)	YMC-Triart C8, 3 µm, 100 X 3.0 mmI.D. (L/dp = 33,300)	YMC-Triart C8, 1.9 µm, 50 X 2.0 mmI.D. (L/dp = 26,300)
Eluent	solution A*/acetonitrile (29/11) **Dissolve 0.725 g of $NaH_2PO_4 \cdot 2H_2O$ and 4.472 g of Na_2HPO_4 in 300 mL of water, and dilute with water to 1000 mL. Dilute 250 mL of this solution with water to 1000 mL. If necessary, adjust with H_3PO_4 to a pH of 7.6.*			
Flow rate	0.8-1 mL/min	1.0 mL/min	0.7 mL/min	0.5 mL/min
Temperature	No description	45℃		
Detection	UV at 280 nm			
Injection volume	50 µL	20 µL**	6 µL	1 µL
System suitability requirement	Rs (1, 2) ≥ 3.0			

**Maximum injection volume of the equipment used

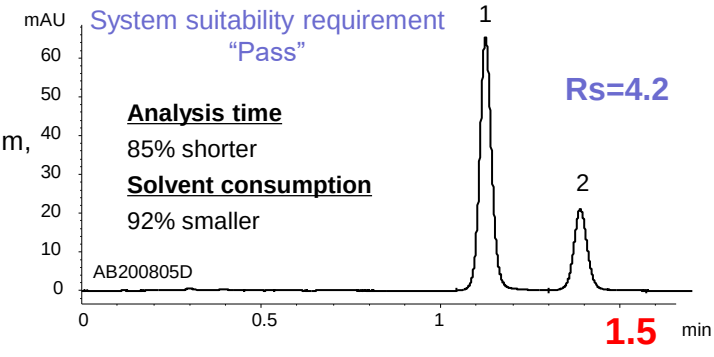
【USP-compliant】
YMC-Triart C8, 5 µm,
150 X 4.6 mmI.D.
1.0 mL/min
(Response: 1 sec)



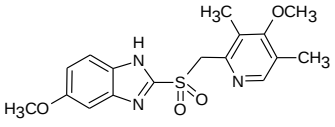
【HPLC】
YMC-Triart C8, 3 µm,
100 X 3.0 mmI.D.
0.7 mL/min
(Response: 1 sec)



【UHPLC】
YMC-Triart C8, 1.9 µm,
50 X 2.0 mmI.D.
0.5 mL/min
(Response: 0.13 sec)

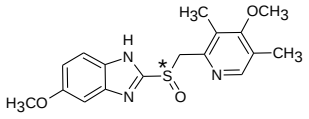


1.



Omeprazole related compound A
(Omeprazole sulfone)

2.



Omeprazole

Particle size and column inner diameter were changed to 3 µm and 3.0 mm, respectively. Thus, the column length was set to 100 mm based on L/dp within the permissible range.

The analysis time was shortened by 60% and solvent consumption was reduced by 70% while meeting the system suitability requirement.

Under UHPLC conditions using a YMC-Triart C8, 1.9 µm, 50 X 2.0 mmI.D. column, analysis time and solvent consumption were reduced by approximately 85–90% while meeting the system suitability requirement and maintaining the resolution requirement of ≥3.0.

With UHPLC, it is important to minimize instrument dead volume and to optimize detection parameters such as data acquisition speed (response).

In the analysis of Esomeprazole Magnesium, both the USP-compliant and time-saving conditions permitted by the International Harmonization of Pharmacopoeias met the system suitability requirement.

YMC-Triart columns exhibit the same selectivity across different particle sizes, allowing for easy method transfer from HPLC to UHPLC as shown here.