

APPLICATIONS

Analysis of Metformin HCl Using a Luna[®] SCX Ion-Exchange HPLC Column per the USP Monograph

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When not in the lab, Sean enjoys just about anything involving the outdoors; hiking, climbing, surfing, etc. He is especially at home in the mountains, being an avid skier and motorcyclist.



Introduction

Metformin HCl is a prescription medication predominantly used to combat type-2 diabetes. The API decreases glucose production in the liver and increases glucose use by body tissues. Aside from its primary use, metformin HCl is increasingly being used in the treatment of Polycystic ovary syndrome.

Because of its important medical applications, a rapid and robust analytical testing method for metformin is necessary. The United States Pharmacopeia (USP) metformin method requires the use of a L9 type LC column for analysis by ion-exchange chromatography. Luna SCX (L9 type column) was used here to demonstrate the standard metformin USP method as well as an optimized version of the USP method which was developed within the USP allowable adjustments.

Results and Discussion

In an effort to improve upon the USP method for the analysis of metformin HCl, an optimized method that fell within the USP allowable adjustments (**Table 2**) was designed. In order to ensure that the new, optimized method produced acceptable results, the two methods were compared side by side. The first method followed the conditions specified in the metformin HCl USP method which required the use of a Luna 10 μ m SCX column (250 x 4.6 mm) at a flow rate of 1.7 mL/min. The second method was optimized within the USP allowable adjustments and instead used a Luna 5 μ m SCX column (150 x 4.6 mm) at a flow rate of 2.0 mL/min.

Both the optimized (5 μ m) and the USP (10 μ m) methods exceeded the resolution requirement between melamine and metformin HCl ($R_s \geq 10$). The USP (10 μ m) method obtained a R_s value of

27.28 and a metformin HCl retention time of 20.6 minutes. The optimized (5 μ m) method resulted in slightly less resolution (R_s value of 20.36) however the elution time was reduced by nearly half with a metformin HCl elution time of 12.9 minutes (**Table 1**).

LC/UV Conditions

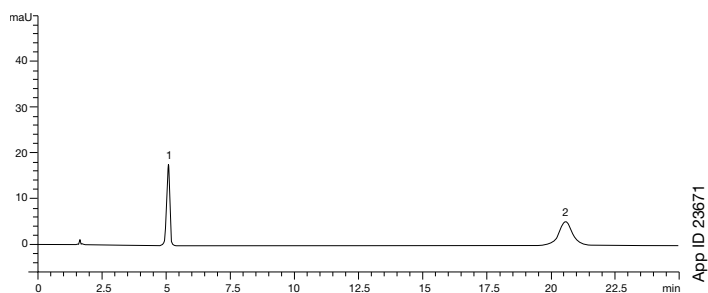
USP Recommended Method:

Column: Luna 10 μ m SCX
Dimensions: 250 x 4.6 mm
Part No.: 00G-4401-E0
Mobile Phase: Ammonium phosphate (17 g/L), pH 3.0
Flow Rate: 1.7 mL/min
Temperature: Ambient
Detection: UV @ 218 nm
Guard column: SecurityGuard[™] Standard SCX 4 x 3.0 mm cartridges (AJ0-4308)
Sample: 1. Melamine
 2. Metformin HCl

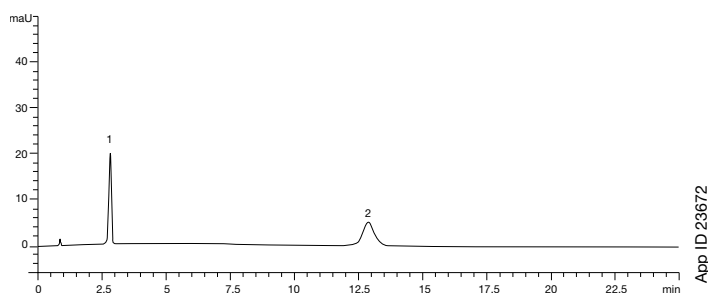
Optimized Method:

Column: Luna 5 μ m SCX
Dimensions: 150 x 4.6 mm
Part No.: 00F-4398-E0
Mobile Phase: No change
Flow Rate: 2.0 mL/min
Temperature: No change
Detection: No change
Guard column: No change
Sample: No change



Figure 1. USP recommended method


App ID 23671

Figure 2. Optimized method


App ID 23672

Table 1. Retention and resolution of metformin HCl

Method	Retention (min)	Resolution (Rs)
Metformin HCl USP Method	20.6	27.28
Metformin HCl Optimized Method	12.9	20.36

Table 2 USP allowable adjustments for isocratic methods

Parameter	Allowable change
Column length	± 70 %
Column ID	Any (const. velocity)
Particle size	- 50 %
Flow rate	± 50 %
Temperature	± 10 %
Mobile phase pH	± 0.2 unit
mM buffer	± 10 %
Injection volume	Any reduction
Wavelength	0 but ± 3 nm between detectors
Mobile phase A/B ratio	Minor ± 30 % relative, but ≤ ± 10 % absolute

Conclusion

As demonstrated, the Luna[®] SCX ion-exchange HPLC column displays symmetrical peak shape and excellent resolution for the USP related substances assay. By optimizing the standard metformin HCl USP method within the USP's allowable adjustments, the analysis time is significantly reduced while still maintaining excellent resolution and peak shape.

Luna[®] SCX HPLC Column Ordering Information

5 µm MidBore™, Analytical, and SemiPrep Columns (mm)							SecurityGuard™ Cartridges (mm)		
Phases	150 x 3.0	50 x 4.6	100 x 4.6	150 x 4.6	250 x 4.6	250 x 10	4 x 2.0*	4 x 3.0*	10 x 10**
SCX	00F-4398-Y0	00B-4398-E0	00D-4398-E0	00F-4398-E0	00G-4398-E0	00G-4398-N0	AJ0-4307 for ID: 2.0-3.0 mm	AJ0-4308 3.2-8.0 mm	AJ0-7369 9-16 mm

10 µm Analytical and Semi-Prep Columns (mm)			SecurityGuard™ Cartridges (mm)	
Phases	250 x 4.6	250 x 10	4 x 3.0*	10 x 10**
SCX	00G-4401-E0	00G-4401-N0	AJ0-4308 for ID 3.2-8.0 mm	AJ0-7369 9-16 mm

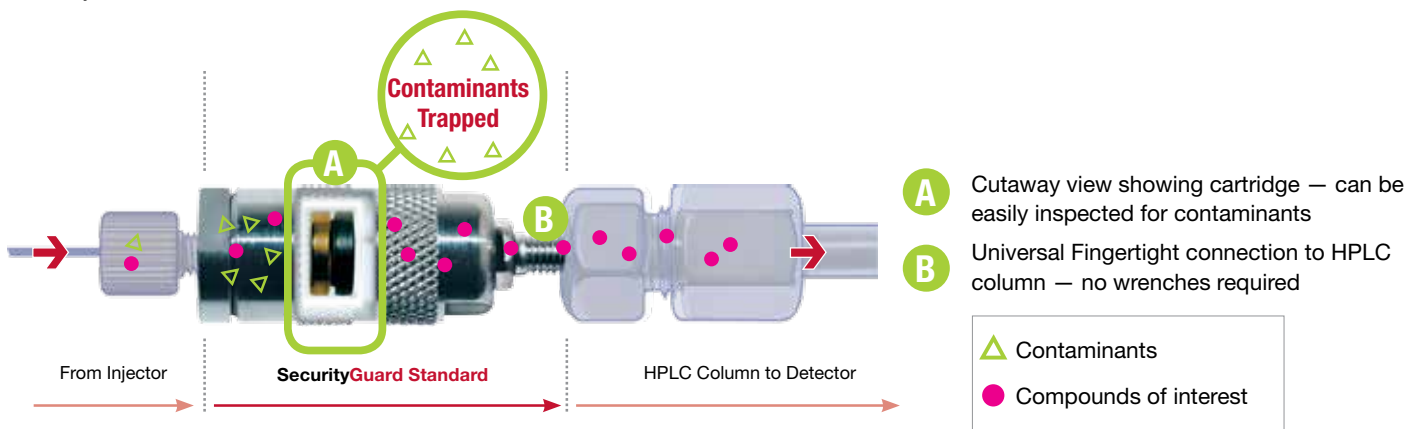
*SecurityGuard Standard Analytical Cartridges require holder, Part No.: KJ0-4282
**SecurityGuard Standard SemiPrep Cartridges require holder, Part No.: AJ0-9281



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