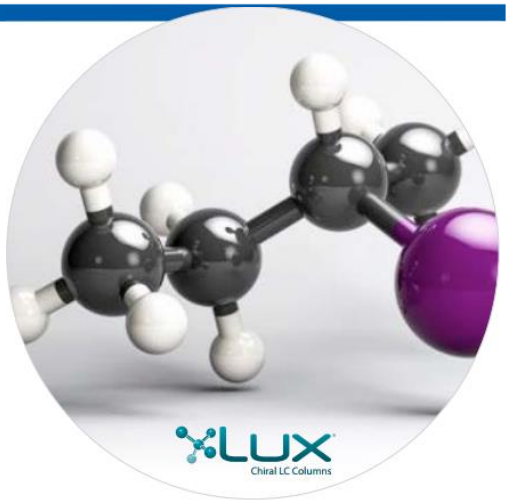

Separation of Solifenacin Succinate Stereoisomers per USP Monograph using Lux® 5 µm Amylose-1 Column

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Overview

Solifenacin Succinate is a chiral drug which is commercialized as pure stereoisomer. It is an anticholinergic drug used for the treatment of patients with overactive bladder. The current trend is to commercialize drugs formulated in their pure stereoisomeric form, which means containing only the single stereoisomer responsible for pharmaceutical activity. The (R,S)-stereroisomer of Solifenacin Succinate is the active form and therefore isolating it from the other stereoisomers is of key importance.

In this application note, we report the stereoisomeric separation between Solifenacin Succinate and its stereoisomers using the Lux Amylose-1 chiral column according to the USP monograph for Solifenacin Succinate. The USP Monograph suggests an ambient running temperature, but we used a lower temperature of 15 °C to help with peak shape, staying within the allowable adjustments per USP <621>.

System suitability per USP Monograph for Solifenacin Succinate is for resolution of not less than (NLT) 1.5 between the Solifenacin (R,S)-stereoisomer and the (S,S)-stereoisomer peaks, and NLT 2.0 between the (R,R)-stereoisomer and Solifenacin Succinate peaks. The separation of the stereoisomers was achieved and peaks corresponding to the (R,S)- and (S,S)-stereoisomers had a resolution of 7.92, and the peaks corresponding to the (R,R)-stereoisomer and Solifenacin Succinate had a resolution of 13 (**Figure 1**). These far surpassed the required resolution to meet system suitability. The higher resolution indicates the powerful chiral recognition ability of the Lux 5 µm Amylose-1 chiral column.

The percent relative standard deviation (%RSD) of the six replicate injections of the Standard Solution must be no more than (NMT) 10.0 % to meet system suitability requirements. All parameters had a %RSD less than 10.0 %, meeting system suitability requirements (**Figure 2**).

All reference solutions were prepared as indicated in the USP Monograph for Solifenacin Succinate. Solifenacin Identification Mixture B RS (Catalog No. 1615322), and Solifenacin Succinate RS (Catalog no. 1615300) were purchased from USP.

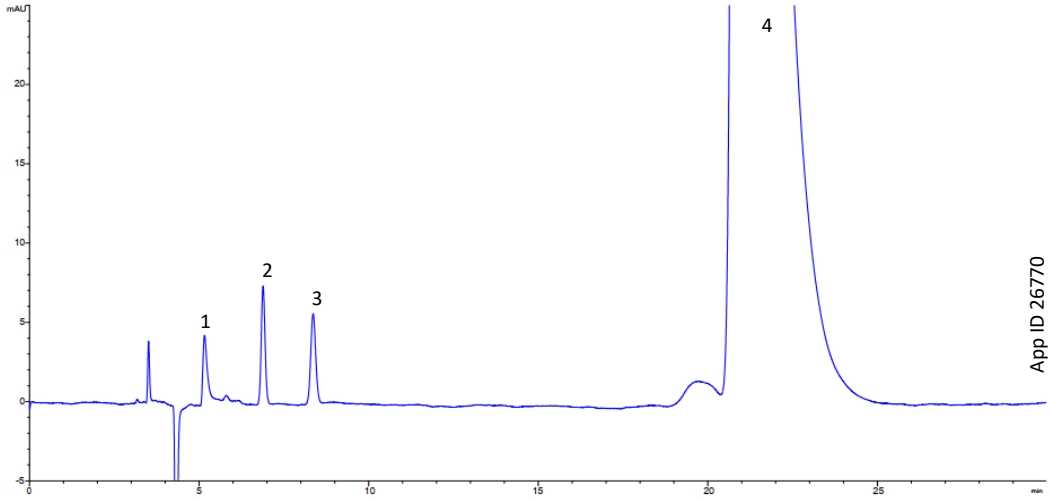
LC-UV Conditions

Column: Lux 5 µm Amylose-1 (250 x 4.6 mm)
Part No.: 00G-4732-E0
Mobile Phase: Chromatographic n-Heptane:Absolute Alcohol: Diethylamine (800:200:1, v/v/v)
Pressure (bar): 76
Flow Rate: 0.8 mL/min
Injection: 10 µL
Temperature: 15 °C
Detector: UV @ 220 nm
System: Agilent® 1260 Binary UHPLC

Table 1. Preparation of Solutions

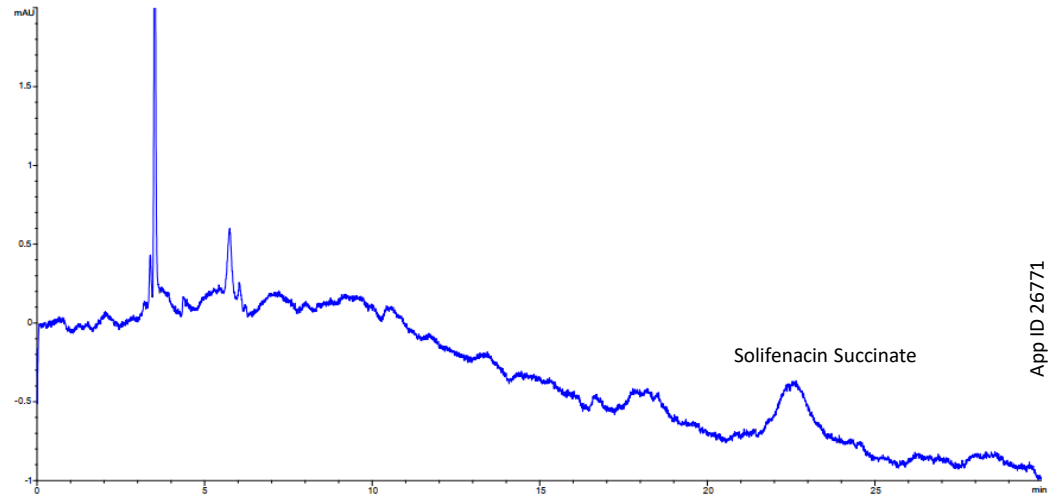
Solution	Composition
System Suitability Solution	Dissolve 2 mg of USP Solifenacin Identification Mixture B RS in 1 mL mobile phase
Standard Solution	Dissolve 1 mg of USP Solifenacin Succinate RS in 1 mL of mobile phase and making a 1:500 dilution of the 1 mg/mL solution to produce a 0.002 mg/mL solution

Figure 1. System Suitability Solution



Peak	Analyte	Resolution
1	(R,S)-Stereoisomer	**7.92**
2	(S,S)-Stereoisomer	
3	(R,R)-Stereoisomer	**13.00**
4	Solifenacin Succinate	

Figure 2. Standard Solution



	Time	Area	Height	Width
AVG	22.655	21.450	0.330	1.093
STD	0.188	1.912	0.029	0.100
%RSD	**0.830**	**8.913**	**8.783**	**9.141**
Number of injections = 6				

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