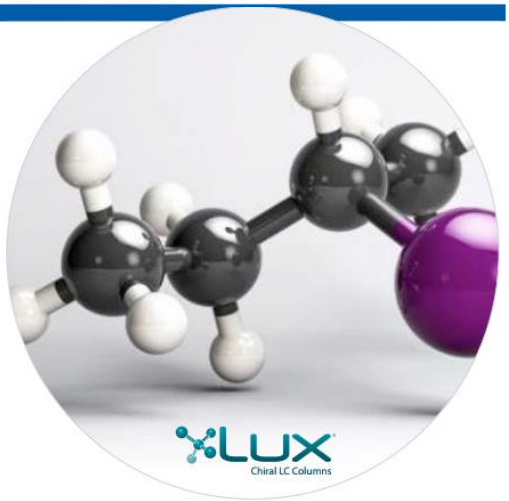

Chiral Purity Testing of the Drug Substance Rivaroxaban Using Lux® 5 µm Cellulose-1 Chiral Column as per USP Monograph

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Overview

Rivaroxaban is a small molecule chiral drug used as an anticoagulant to treat blood clots. It is commercialized as the pure S-enantiomer. Separation of the enantiomers of chiral drugs has become of vital importance in analytical chemistry in recent years, because of differences in the biological activity and pharmacokinetic properties of drug enantiomers.

In this application note, we demonstrate the successful enantiomeric separation between Rivaroxaban and its enantiomer impurity, R-enantiomer, using the Lux Cellulose-1 chiral HPLC column according to the current USP monograph for Rivaroxaban.

System suitability per USP Monograph for enantiomeric purity of Rivaroxaban is for resolution of not less than (NLT) 1.5. The separation of the enantiomers was achieved and peaks corresponding to the R-enantiomer and Rivaroxaban had a resolution of 2.37, exceeding the system suitability requirement (**Figure 2**). The higher resolution indicates the powerful chiral recognition ability of Lux 5 µm Cellulose-1 chiral column.

The monograph for enantiomeric purity also requires a symmetry factor of not more than (NMT) 1.5 for the peak associated with Rivaroxaban. Lux 5 µm Cellulose-1 easily provided a symmetry factor of 1.24, meeting system suitability.

All reference solutions were prepared as indicated in the USP Monograph for Rivaroxaban. USP Rivaroxaban RS (Catalog No. 1604530), and USP Rivaroxaban R-Enantiomer RS (Catalog no. 1604541) were purchased from USP.

LC-UV Conditions

Column: Lux 5 µm Cellulose-1 (150 x 4.6 mm)
Part No.: 00F-4459-E0
Mobile Phase: Ethanol and Heptane (30:70)
Pressure (bar): 69
Flow Rate: 1 mL/min
Injection: 15 µL
Temperature: 50 °C
Detector: UV @ 250 nm
System: Agilent® 1260 Binary UHPLC

Preparation of Solution

System Suitability Solution : 0.4 mg/mL of USP Rivaroxaban RS and 0.004 mg/mL of USP Rivaroxaban R-Enantiomer RS prepared as follows. To a suitable volumetric flask add a suitable amount of USP Rivaroxaban RS and USP Rivaroxaban R-Enantiomer RS. Add acetonitrile to about 50% of the flask volume, and dilute with ethanol to volume.

Figure 1. Rivaroxaban Chemical Structure

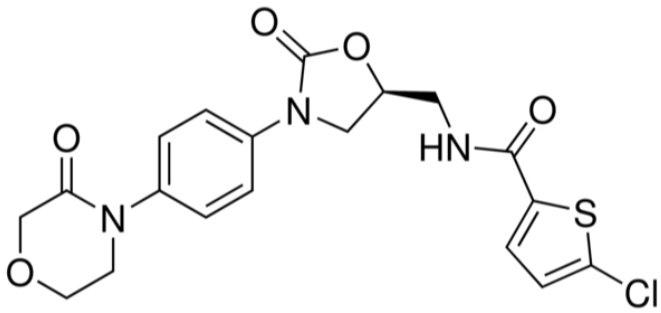
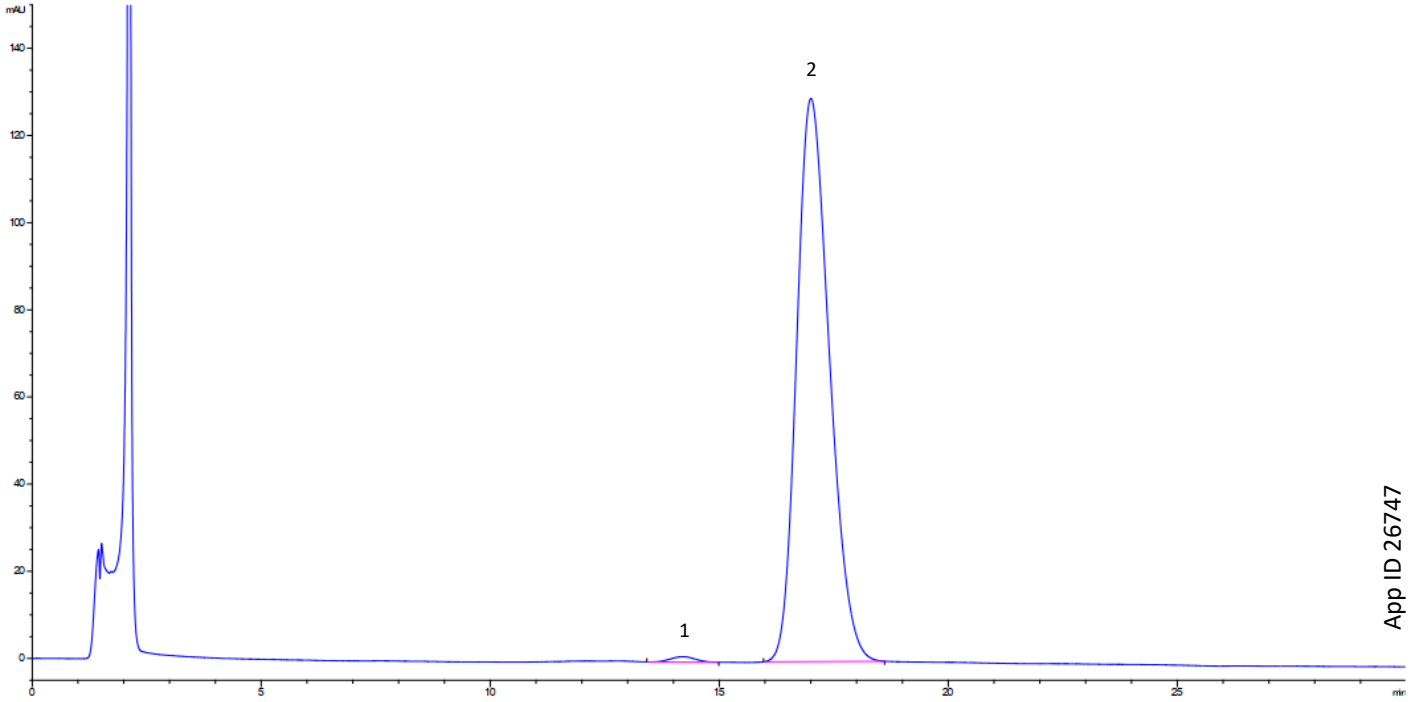
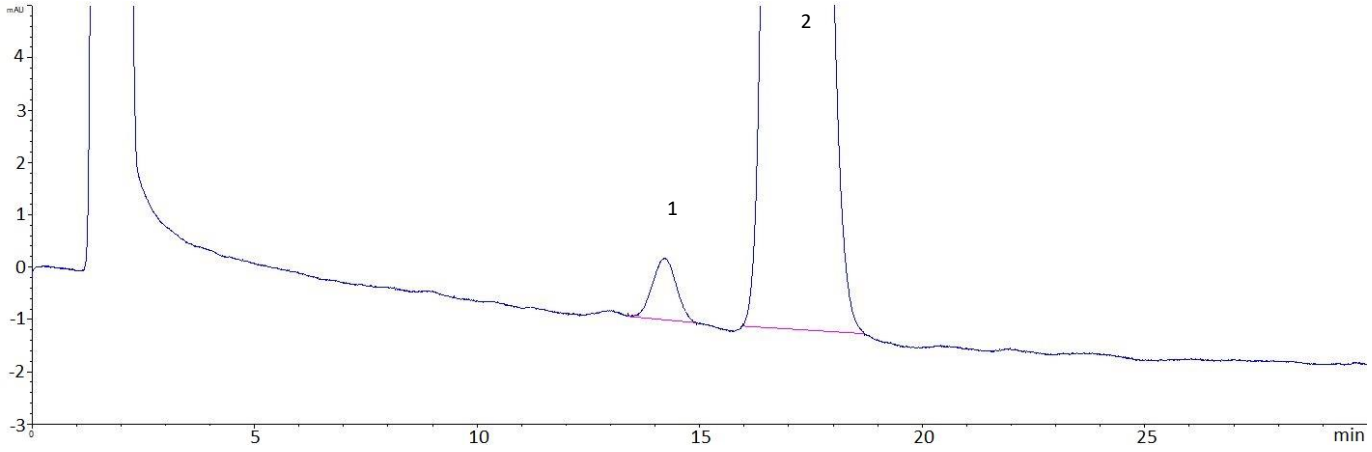


Figure 2. Resolution of Ricaroxaban R-Enantiomer (1) and Rivaroxaban (2)



No.	Peak	Time	Area	Height	Width	Symmetry Factor	Resolution
1	Rivaroxaban R-enantiomer	14.1	50.6	1.3	0.65		2.37
2	Rivaroxaban	17.0	6427.3	128.5	0.68	1.24	

Figure 3. Zoomed-in View of Chromatogram to Highlight Resolution



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