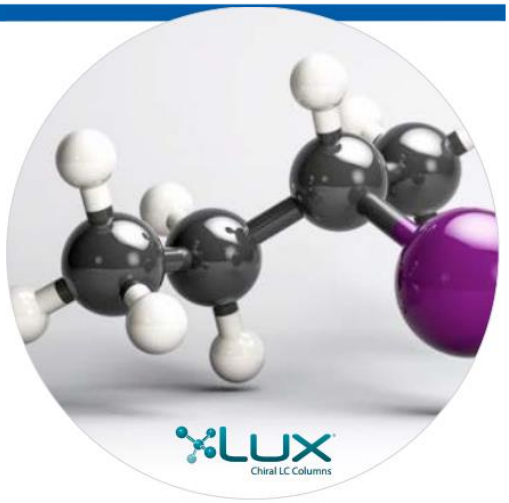

Chiral Separation of the Drug Product Lacosamide on a Lux® 5 µm Amylose-1 Column According to Ph. Eur. Monograph 2992

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Overview

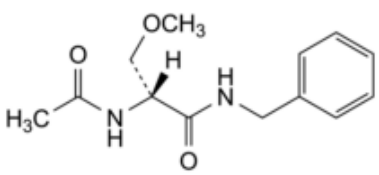
Lacosamide is a chiral drug which is commercialized as pure enantiomer. It is an antiepileptic drug approved in the USA and Europe. The current trend is to commercialize drugs formulated in their enantiopure form, which means containing only the enantiomer responsible for the pharmaceutical activity. The S-enantiomer of Lacosamide, designated as Impurity A, is pharmaceutically inactive and therefore undesirable to have in the presence of the active R-Lacosamide.

In this application note, we report the enantiomeric separation between Lacosamide and its enantiomer (Impurity A) using the Lux Amylose-1 chiral column according to the Ph. Eur. Monograph 2992.

System suitability per Ph. Eur. Monograph 2992 for enantiomeric purity of Lacosamide is for resolution of not less than (NLT) 3.0. The separation of the enantiomers was achieved and peaks corresponding to the Impurity A and Lacosamide had a resolution of 4.7, exceeding the system suitability requirement (**Figure 2**).The higher resolution indicates the powerful chiral recognition ability of Lux 5 µm Amylose-1 chiral stationary phase column.

All reference solutions were prepared as indicated in Ph. Eur. Monograph 2992 for Lacosamide. Lacosamide Certified Reference Standard (CRS), (Catalog No Y0001982) and Lacosamide Impurity A CRS (catalog no. Y0001972) were purchased from the European Directorate for the Quality of Medicines & HealthCare (EDQM) Council of Europe.

Figure 1.
Lacosamide



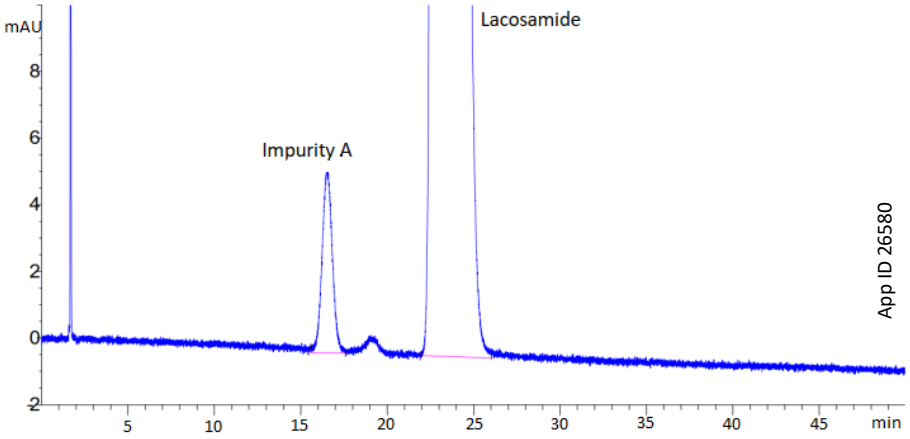
LC-UV Conditions

Column: Lux 5 µm Amylose-1
Dimensions: 150 x 4.6 mm
Part No.: 00F-4732-E0
Mobile Phase: Water, 2-Propanol, Heptane (3:100:900, v/v/v)
Pressure (bar): 81
Flow Rate: 1 mL/min
Injection: 20 µL
Temperature: 25 °C
Detector: UV @ 215 nm
System: Agilent® 1260 Binary UHPLC

Table 1. Preparation of Test and Reference Solutions

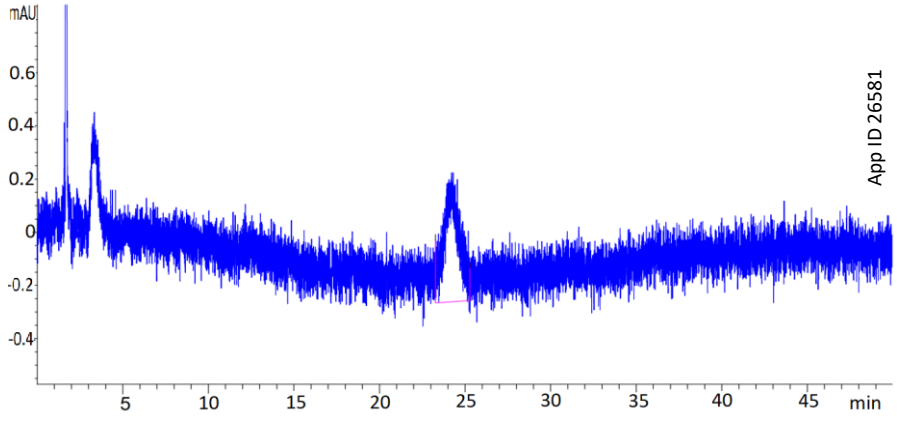
Solution	Composition
Test Solution	Dissolve 50.0 mg of the substance to be examined in the mobile phase (MP) and dilute to 50.0 mL with MP
Reference Solution (a)	Dissolve 1 mg/mL of Lacosamide Impurity A CRS in MP and dilute to 10.0 mL with MP.
Reference Solution (b)	Dissolve 20 mg of the substance to be examined in MP, add 1.0 mL of reference solution (a) and dilute to 20.0 mL with MP.
Reference Solution (c)	Dilute 1.0 mL of the test solution to 100.0 mL with MP. Dilute 1.0 mL of this solution to 20.0 mL with MP.

Figure 2. System Suitability Solution (Reference Solution (b))



Peak	Time	Area	Height	Width	Resolution
Impurity A	16.5	225	5.5	0.6	4.7
Lacosamide	23.1	37231	556.6	99.4	

Figure 3. Reference Solution (c): 0.5 µg/mL of Lacosamide CRS



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