eksigent

application note

use of the expressLC™ system for chiral drug analysis

rapid, high resolution, normal phase isocratic chiral separations

introduction

Conventional carbon-centered enantiomericity has become a major aspect of pharmaceutical drug development over the last twenty years. Although enantiomeric drug forms have long been known to exist, attention to the relative bioactivity of the enantiomers was often not addressed. More recently, drug manufacturers have investigated the pharmacological profiles of the individual isomers, and in some cases, found that the bioactivity of the drug substance could be wholly or substantially attributed to a single enantiomer.

figure 1. chromatogram of the two enantiomers of fenoprofen

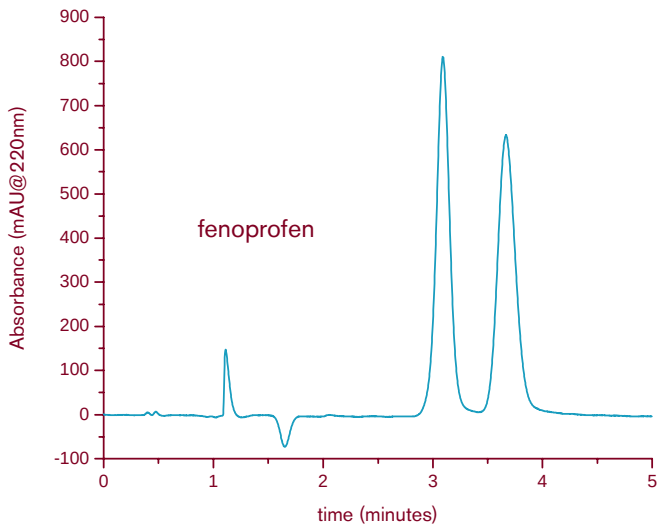
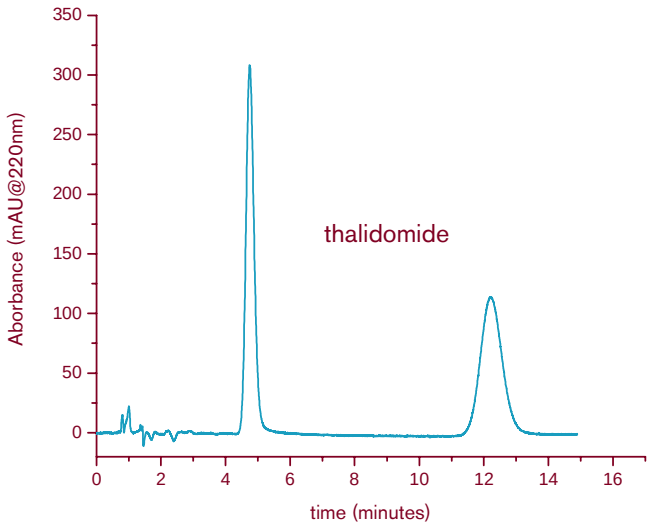


figure 2. chromatogram of the two enantiomers of thalidomide



experimental conditions

chiral analysis

Increased sophistication of LC chiral analysis has come to the forefront of pharmaceutical analysis, including analysis of atropisomeric (hindered rotation around a single bond) species. Often, the limited availability of pure enantiomers, high cost of convention LC columns, low peak efficiencies (and resulting high detection limits of the minor chiral species), lengthy analysis times, and frequent conversion to normal phase chromatography has made pharmaceutical chiral analysis an analytical specialty field unto itself. As shown in the figures 1-4, the ExpressLC system delivers chiral analysis of drugs of pharmaceutical interest, often within 5 minutes, with efficient peaks, and very low sample size requirements. In addition, the ExpressLC system allows rapid and convenient conversion between normal- and reversed-phase eluents. The very low stationary and mobile phase volume requirements for the ExpressLC system allow analytically unique and potentially powerful chromatographic conditions unavailable in a conventional chromatography format.

Instrument:	ExpressLC System
Column:	Chiral Technologies AD-H stationary phase, 150 x 0.32 mm, 5 µm particle
Mobile phase:	A/B heptane/2-propanol 0.1% acetic acid
Flow rate:	10 µL/minute

species	A:B (%)	injection (µL)
fenoprofen	95:5	80
thalidomide	50:50	40
warfarin	80:20	100
5-methyl-5-phenylhydantoin	80:20	100

figure 3. chromatogram of the two enantiomers of warfarin

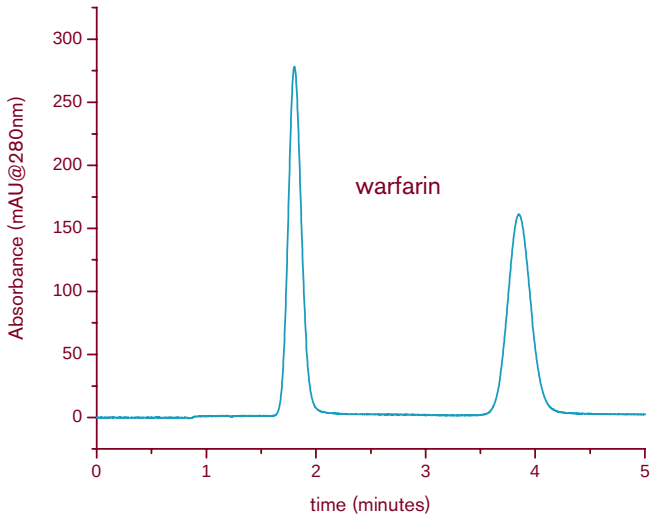
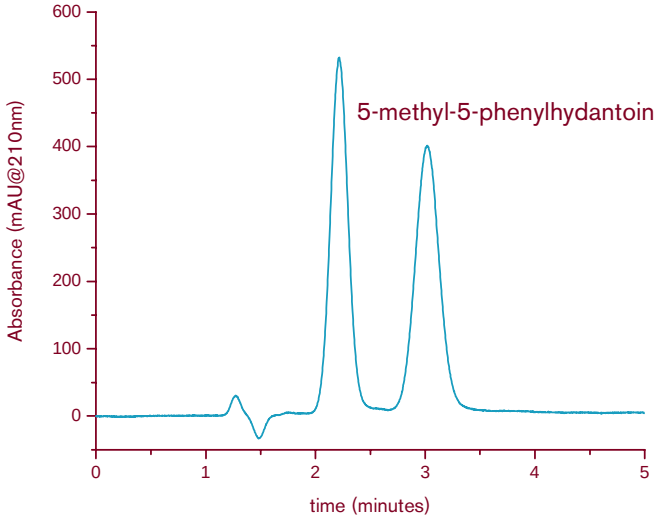


figure 4. chromatogram of the two enantiomers of 5-methyl-5-phenylhydantoin



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expressLC system specifications

configuration

expressLC-100 Single-channel System: Includes binary gradient pump, electronic injection valve, column temperature control, and array-based UV detection system. Optional high-speed autosampler available.

expressLC-800 8-channel Parallel System: Includes 8 binary gradient pumps, 8 electronic injection valves, 8 column temperature control compartments, an array-based UV detection system and high-throughput autosampler.

flow rate range
0.20–30 µL/min

pump type
Microfluidic direct pumping system with independent flow control feedback for each mobile phase. Retention time RSD < 0.5%.

gradient formation
High pressure gradient mixing. System can run full gradients as rapidly as 8 seconds. Maximum gradient length 2 hrs. at 5 µL/min.

delay volume
< 500 nL from mixer to column.

mobile phase compatibility
All mobile phases compatible with 316 stainless steel, PEEK, and silica.

injection valve
Eksigent Variable-Volume Injection System (software selectable). Standard injection volume 10–250 nL (larger injection volumes available).

columns
System optimized for 2.5–15 cm, 300 µm i.d. capillary LC columns

column temperature control
Software selectable from 27–40°C; stability within ± 0.1°C

detection
UV absorbance detection from 200–380 nm using linear CCD array detector. Detector drift ≤ 4 x 10^{-4} AU/hr Non-linearity ≤ 5% @ 2 AU.

flow cell
45 nL microfabricated flow cell with integral fiber optics, 4 mm path length

autosampler
High-throughput CTC autosampler available

system control
Computer with graphical user interface for control of all system parameters. Software allows import of run tables and creates CDF, text, and Excel files for data export and analysis. Tracking of instrument runtime, column usage, total injections, solvent usage, lamp hours, and error codes. System drivers available for Thermo Electron's Xcalibur and Applied Biosystems/MDS SCIEX Analyst 1.4.1 mass spectrometer software.

report features
Generates reports that include method conditions, chromatograms, peak retention times and areas, and spectral absorbance map.

dimensions
expressLC-100 System:
21" (53 cm) wide, 20" (51 cm) deep, 18" (46 cm) high
expressLC-100 Autosampler:
Additional 14" (36 cm) high and 6" (15 cm) wide
expressLC-800 System:
30" (76 cm) wide, 34" (86 cm) deep, 40" (102 cm) high
expressLC-800 Autosampler:
Additional 16" (41 cm) high and 16" (41 cm) wide
computer
Additional lab space needed for keyboard, mouse and monitor

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