

# The Semba Octave™ Chromatography System

The Power of Simulated Moving Bed Chromatography on Your Bench

## Application Note 1: Continuous Chiral Separation

Single-enantiomer active pharmaceutical ingredients (APIs) have come to dominate the list of blockbuster drugs. As of 2005, the six of the seven top-selling drug formulations were single-enantiomer products (1). At present, the FDA imposes stringent rules on chiral purity of the final APIs; this has a big impact on development of new chiral drugs. The biological activity of the pure enantiomers has to be evaluated early in the pre-clinical, lead optimization stage of drug discovery, and small amounts of each enantiomer (milligrams to grams) have to be obtained. Ideally, the methods used to produce required amounts of a chiral drug in the pre-clinical phase should be transferable to larger scale chiral API production.

The Simulated Moving Bed Chromatography (SMBC) process has been successfully utilized in the large-scale production of several pure enantiomer APIs, including one of the top-selling drugs manufactured by Pfizer, Zolofit (2). The same benefits SMBC brings to large scale chromatography are realized on the smaller scale with the Semba Octave™ Chromatography System. The following example demonstrates separation of a (+)/(-) 5-methyl 5-phenylhydantoin racemic mixture into two pure enantiomers using the Semba Octave™ System and Astec CHIROBIOTIC™ V2 chiral stationary phase columns.

**Columns:** 8 x Astec CHIROBIOTIC™ V2,  
5 cm x 10 mm, 15 μ

**Sample:** 5-methyl 5-phenylhydantoin  
racemate (selectivity = 1.39)

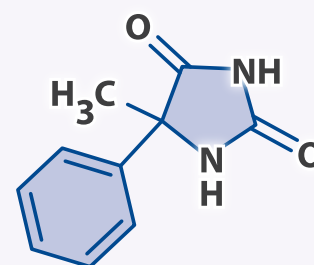
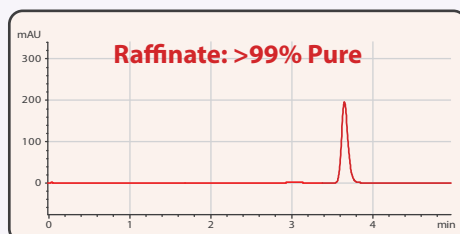
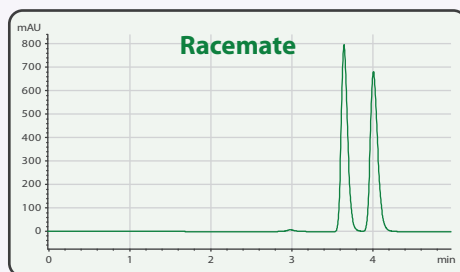
**Purification:** 3-2-3 SMBC

**Feed concentration:** 10 mg/ml

**Desorbent:** 100% MeOH

**Recovery:** 90%

**Productivity:** >35 mg/h each enantiomer



### Separation of (+)/(-) 5-methyl 5-phenylhydantoin enantiomers

Enantiomers were separated using the indicated Astec CHIROBIOTIC™ V2 columns on the Semba Octave™ System in a 3-2-3 SMBC configuration. Samples of Feed (Racemate), Raffinate, and Extract were analyzed by HPLC on an Astec CHIROBIOTIC™ V2 25 cm x 4.6 mm, 5 μ column using 100% MeOH as eluent.

1. Van Arnum, P. (2006) *Pharm. Technol.* **29** (4), 58-66.
2. McCormick, D. (2006) *Pharm. Technol.* **30** (5), 24-29.

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