ZirChrom®-MS Exhibits Unique Selectivity for Basic Pharmaceuticals

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Technical Bulletin #299

Basic pharmaceuticals are well-known problematic compounds on silica C18 due to the interactions between the amine functionalities and non-bonded residual silanol groups[1]. In this application note we demonstrate the utility of a new Lewis acid deactivated zirconia-based column, ZirChrom®-MS. The new ZirChrom®-MS column exhibits unique selectivity for the specific set of amine-containing compounds studied.

Introduction

The chromatography of basic pharmaceuticals on silica C18 has traditionally been so problematic that amitriptyline is commonly used as a probe solute for quantifying silanophilicity of silica phases. The surface chemistry of zirconia-based phases is dominated by Lewis acid sites, rather than the Bronsted acid sites, which dominate the surface chemistry of silica phases. The mixed-mode retention character of ZirChrom®-MS (cation-exchange and reversed-phase) allows separations that were previously difficult using conventional silica C18 phases.

Using traditional, near normal pH operating conditions one typically obtains significantly higher retention for basic compounds on ZirChrom®-MS versus traditional silica C18. Even though there is much higher carbon loading to silica-based columns the strong ion-exchange contribution to retention results in an overall higher retention factor on the ZirChrom®-MS column. In fact, the ZirChrom®-MS phase has relatively higher retention for basic drugs compared to all of the zirconia-based reversed phases as well. In general, excellent peak shapes may be obtained using LC/MS compatible, near neutral pH operating conditions.

In addition, ZirChrom®-MS enables the user to analyze basic pharmaceutical compounds, acidic pharmaceutical compounds, or both simultaneously, under LC/MS compatible, near neutral pH operating conditions.

Experimental

The selectivity of a set of basic pharmaceuticals was compared using a leading silica C18 column and a ZirChrom®-MS column. The separation conditions were as follows:

Column Size:	50 mm x 4.6 mm i.d.
Mobile Phase:	Isocratic elution: 65/35 A/B A: methanol B: 25mM ammonium phosphate, pH 6.0
Temperature:	35 ºC
Flow Rate:	1.0 ml/min.
Injection Vol.:	5 µl
Detection:	UV at 254 nm
Solutes:	(From left to right in **Figure 1**) Methapyrilene, Pyrilamine, Tripelennamine, Brompheniramine, Desipramine, Nortryptyline, Doxepin, Amitryptyline

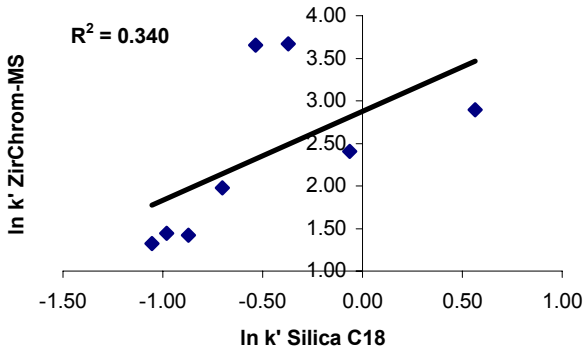

Figure 1: Selectivity Comparison for a Set of Basic Pharmaceuticals - leading Silica C18 versus ZirChrom®-MS.

As a result of the mixed-mode ion-exchange and reversed-phase characteristics of ZirChrom®-MS, the elution order of basic pharmaceuticals is often quite different compared to leading reversed-phase silica phases. **Figure 1** shows a plot of ln k' for eight common basic pharmaceuticals on a leading silica C18 phase versus ln k' for the same compounds on ZirChrom®-MS. There is no apparent correlation of the retention for these compounds on the silica C18 phase with the retention on ZirChrom®-MS. This different selectivity is particularly useful in method development for basic pharmaceuticals. When a pair of basic compounds cannot be separated using a traditional silica C18 phase, the chances of them separating on ZirChrom®-MS are much better than on any other silica phase.

This method can be tailored to your specific application needs. ZirChrom method developers can help to optimize and transfer this method to your site. Please contact ZirChrom technical support at 1-866-STABLE-1 or support@zirchrom.com for details.

ZirChrom phases offer unique selectivity, high efficiency, and excellent chemical and thermal stability.

References

1) G.B. Cox, *J. Chromatography A*. **656**, 353, 1993.

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