

Gradient SFC Separation of Pharmaceutical Compounds using a Polyvinyl Alcohol Stationary Phase

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TESTING COLUMN SELECTIVITY?

The following drug-like compounds were used for testing:

Table 2. Initial Selection of Study Columns Used With Standard Elution Method (Figures 1a and 1b)











Introduction

YMC Co., Ltd, Kyoto, Japan has been offering covalently bonded phases for normal phase high performance liquid chromatography (HPLC) for over 25 years. The use of diol, cyano, and amino functional groups bonded to silica offered a number of technical advantages to bare silica for normal phase HPLC. More recently newer phases bonded to silica like 2-ethyl pyridine¹ and similar products have brought different new selectivity options for chemists practicing SFC. The work cited below shows the ability of a polyvinyl alcohol phase for offering new selectivity options for separation of pharma and pharma-like molecules.

Notes:

1. Princeton Chromatography.
2. All experimental work was performed by: America Discovery Sciences, Inc. One Innovation Drive Three Biotech Worcester, MA 01605 USA

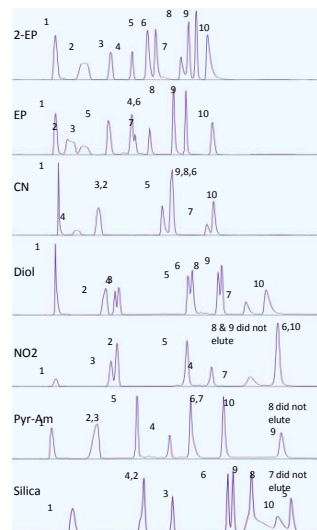
Table 1. Drug-Like Compounds Used in the Test Standard

Compound (elution order on 2-EP)	Name	
1	Citral	
2	Lidocaine	
3	Caffeine	
4	Ibuprofen	
5	Amitriptyline	
6	Propranolol	
7	Procainamide	
8	Sulpiride	
9	b-D-Arabinofuranosyl-cytosine	
10	Sulfrinpyrazone	

The test standard was injected onto each column using an SFC gradient method of 5%-65% cosolvent in CO₂ (total flow of 2.0 mL/min) over 5 or 12.5 minutes, (depending on column length) followed with a 10 second hold at 65% and a return to initial condition. The mobile phase cosolvent is 50:50 methanol:isopropanol with 0.1% diethylamine (MeOH:IPA 0.1%DEA).

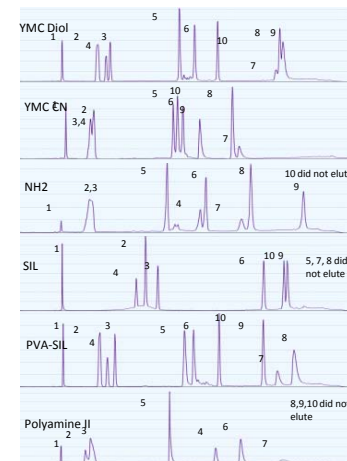
Column	Description
2-EP	2-Ethylpyridine 5 μ , 4.6x100mm, Princeton Chromatography
EP	Ethylpyridine SFC 5 μ , 4.6x100mm, ES Industries
CN	PrincetonSFC CN, 5 μ , 4.6x100mm, Princeton Chromatography
Diol	PrincetonSFC Diol, 5 μ , 4.6x100mm, Princeton Chromatography
NO2	Epic-NO2 SFC, 5 μ , 4.6x100mm, ES Industries
Pyr-Am	Pyridyl Amide SFC, 5 μ , 4.6x100mm, ES Industries
Silica	PrincetonSFC Silica, 5 μ , 4.6x100mm, Princeton Chromatography

Figure 1a. Column Selectivity Study Chromatograms (10 cm, 8 minute gradient)



Column	Description
YMC-Diol	YMC-Pack Diol-120-NP, 4.6 x 250mm, 5 μ m, YMC
YMC-CN	YMC-Pack CN, 4.6 x 250mm, 5 μ m, YMC
NH2	YMC-Pack NH2, 4.6 x 250mm, 5 μ m, YMC
SIL	YMC-Pack SIL, 4.6 x 250mm, 5 μ m, YMC
PVA-SIL	YMC-Pack PVA-SIL-NP, 4.6 x 250mm, 5 μ m, YMC
Polyamine II	YMC-Pack Polyamine II, 4.6 x 250mm, 5 μ m, YMC

Figure 1b. Column Selectivity Study Chromatograms (25 cm, 17 minute gradient)



Conclusions:

1. Unmodified silica is a poor choice for SFC chromatography.
2. Modified silicas show large differences in selectivity.
3. Polyvinyl alcohol phase demonstrates good peak shape and exceptional selectivity for the range of compounds tested (acids, bases, neutrals).
4. Additional work is warranted on the potential use of PVA-Sil for preparative separations.