

# The role of the silanol groups in the separation of basic antidepressants by reversed-phase chromatography



Eidgenössische Technische Hochschule Zürich  
Swiss Federal Institute of Technology Zurich

Nicola Forrer and Massimo Morbidelli

Institute for Chemical and Bioengineering,  
Department of Chemistry and Applied Biosciences,  
ETH Zurich, 8093 Zurich, Switzerland

## 1. Introduction

Six C18 silica based resins were investigated in the ability to separate a mixture of three antidepressants. The resolution between two of them (amitriptyline and imipramine) was used as a performance parameter and related to different structure parameters of the resins.

### Resins investigated

- Kromasil C18
- YMC Gel ODS A
- Nucleodur C18 ec
- Daisogel SP-ODS-BP
- Chromatorex SMB C18
- ZEOSphere C18

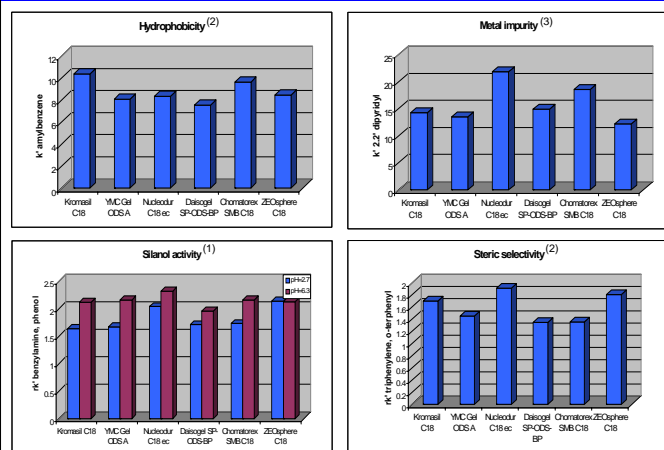
### Structure parameters (1, 2)

- Silanol activity
- Hydrophobicity
- Metal impurity
- Steric selectivity

### Performance parameter

- Resolution between amitriptyline and imipramine

## 2. Structure parameters

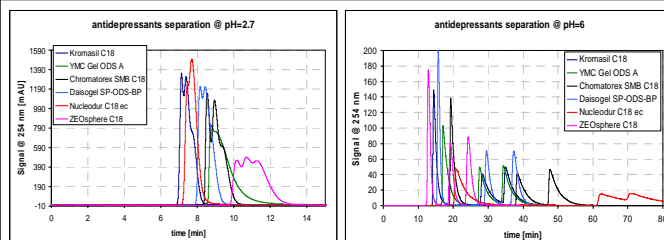


$$\text{Retention factor: } k'_i = \frac{t_{R,i} - t_{0,i}}{t_{0,i}} = \frac{1 - \epsilon_i}{\epsilon_i} H_i$$

$$\text{Relative retention factor: } rk'_{i,j} = \frac{k'_i}{k'_j} = \frac{\frac{1 - \epsilon_i}{\epsilon_i} H_i}{\frac{1 - \epsilon_j}{\epsilon_j} H_j}$$

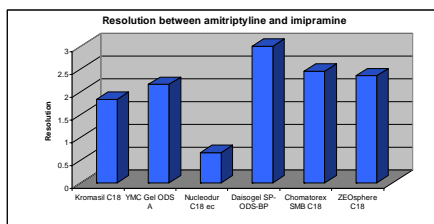
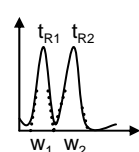
## 3. Performance parameter

Separation of a mixture of three basic tricyclic antidepressants (nortriptyline, amitriptyline and imipramine) at two different pH.



### Resolution between amitriptyline and imipramine @ pH=6

$$R = \frac{2(t_{R2} - t_{R1})}{w_1 + w_2}$$

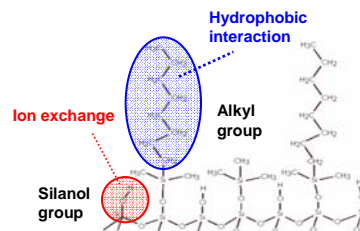


## 4. Solute – stationary phase interaction

Two type of interactions:

**Alkyl groups:** hydrophobic interaction

**Silanol groups:** ion exchange interaction (pH dependent)

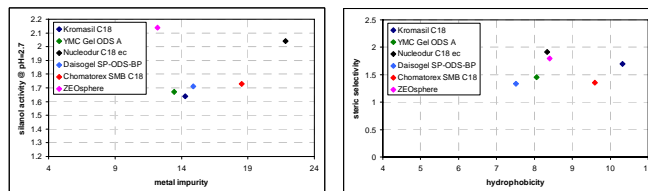


**Low pH:** most of the silanols are protonated → mainly hydrophobic interaction (and hydrogen bonding)

**High pH:** most of the silanols are deprotonated → hydrophobic and ion exchange interactions

## 5. Correlations

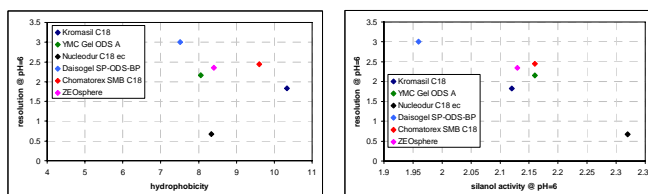
### Between structure parameters



The silanol activity at low pH (very acid silanols) increases for increasing metal impurity.

The steric selectivity increases for increasing hydrophobicity (pore blocking).

### Between structure and performance



The resolution is independent from hydrophobicity.

The resolution at pH=6 decreases for increasing silanols ion exchange strength.

## 6. Conclusions

- Metal impurities are increasing the activity of very acid silanols.
- High hydrophobicity decreases the pore accessibility.
- The resolution between amitriptyline and imipramine is independent on hydrophobicity.
- At high pH the resolution between amitriptyline and imipramine is inversely proportional to the silanol activity.
- At low pH the silanol activity is too low to resolve the antidepressants.
- It exists an optimal silanol activity for this separation.

### Solvent composition:

(1): MeOH : H<sub>2</sub>O : 0.2M H<sub>2</sub>PO<sub>4</sub>, pH=2.7, pH=6 (34:90:10) w

(2): MeOH : H<sub>2</sub>O (317:100) w

[1]: P. Dehouck et al., LC.GC Europe, November 2004

(3): MeOH : H<sub>2</sub>O (34:100) w

[2]: K. Kimata et al., J. Chromatogr. Sci., 27, 721 (1989)