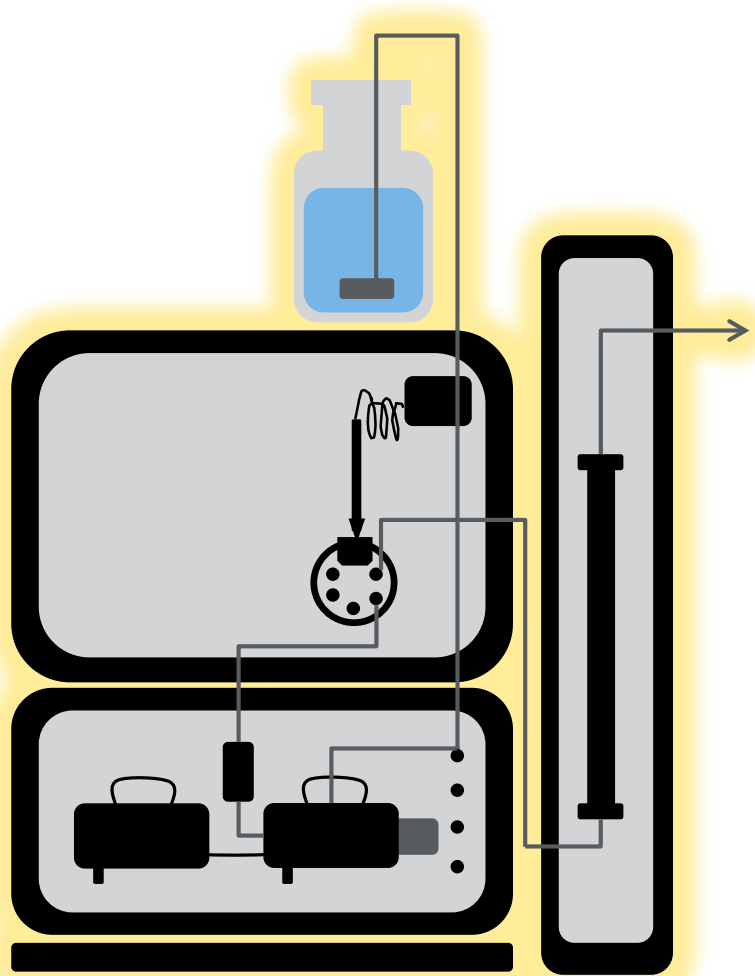


**ThermoFisher**  
S C I E N T I F I C

# Effects of Metal Contamination Caused by Iron-Free HPLC Systems on Peak Shape and Retention of Drugs with Chelating Properties

M. De Pra, G. Greco, N. Bartsch, E. George, M. M. Martin, F. Steiner  
*Thermo Fisher Scientific, Germering (Germany), Bremen (Germany), San Jose (USA)*

# Biocompatible HPLC Systems



- Biocompatible (U)HPLCs are used in the analysis of biomolecules
- Biomolecules are often analyzed with high salt concentrations in the mobile phase
- Conventional stainless steel HPLCs form rust
- In biocompatible UHPLC titanium is used instead of stainless steel

Schematic of fluidic components in a HPLC

**Is titanium always inert?**



## Passive film-induced stress and mechanical properties of $\alpha$ -Ti in methanol solution

Zhi Qin<sup>a</sup>, Xiaolu Pang<sup>a</sup>, Yu Yi<sup>b</sup>

<sup>a</sup>Corrosion and Protection Center, Key Laboratory of Republic of China

<sup>b</sup>Department of Mechanical Engineering, University of Science and Technology Beijing



NASA TECHNICAL NOTE



NASA TN D-6975

CASE FILE COPY

NASA TN D-6975

*Int. J. Electrochem. Sci.*, 9 (2014) 4352–4360

Short Communication

## Correlation Between Properties Corrosion Cracking of $\alpha$ -Ti in N

Zhi Qin<sup>a</sup>, Xiaolu Pang, Lijie Qiao<sup>a</sup>

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DOI: 10.5301/jabfm.5000387

REVIEW



## Corrosion of titanium: Part 1: aggressive environments and main forms of degradation

Davide Prando<sup>1,2</sup>, Andrea Brenna<sup>1,2</sup>, Maria Vittoria Diamanti<sup>1,2</sup>, Silvia Beretta<sup>1,2</sup>, Fabio Bolzon<sup>1,2</sup>, Marco Ormellese<sup>1,2</sup>, Maria Pia Pedferri<sup>1,2</sup>

<sup>1</sup>Department of Chemistry, Materials and Chemical Engineering "G. Natta", Politecnico di Milano, Milan - Italy

<sup>2</sup>National Interuniversity Consortium of Materials Science and Technology, Florence - Italy

## Stress Corrosion Cracking of Ti in pure MeOH

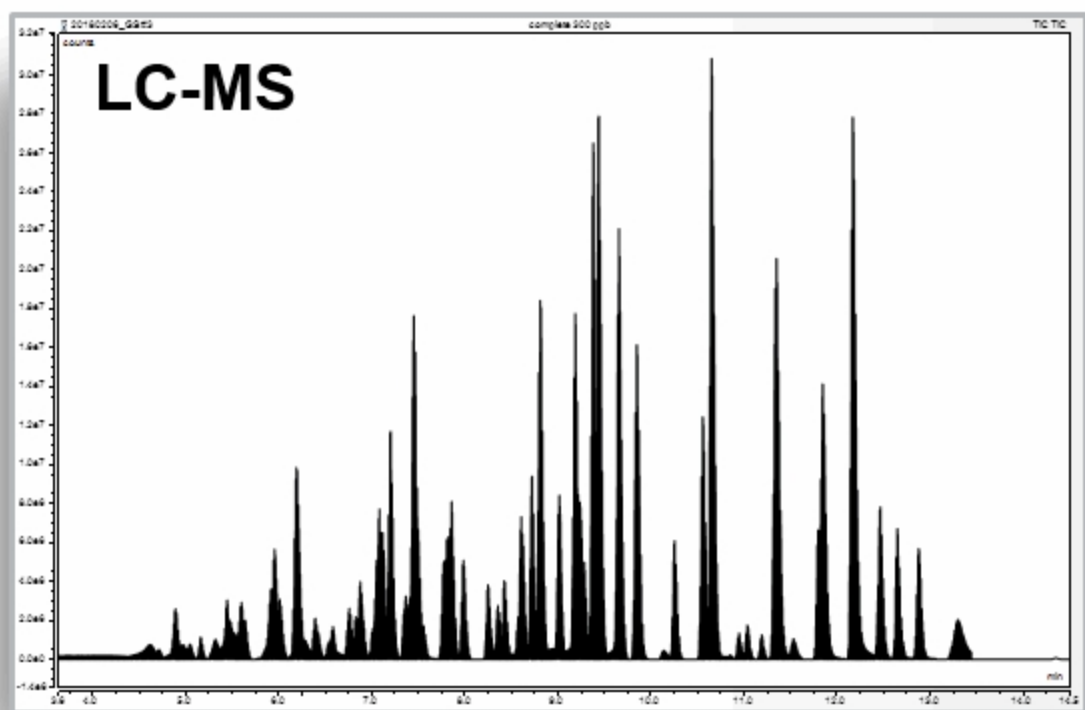
- Relevant problem in material science
- Not a problem for UHPLC systems

Any effect on chromatography?

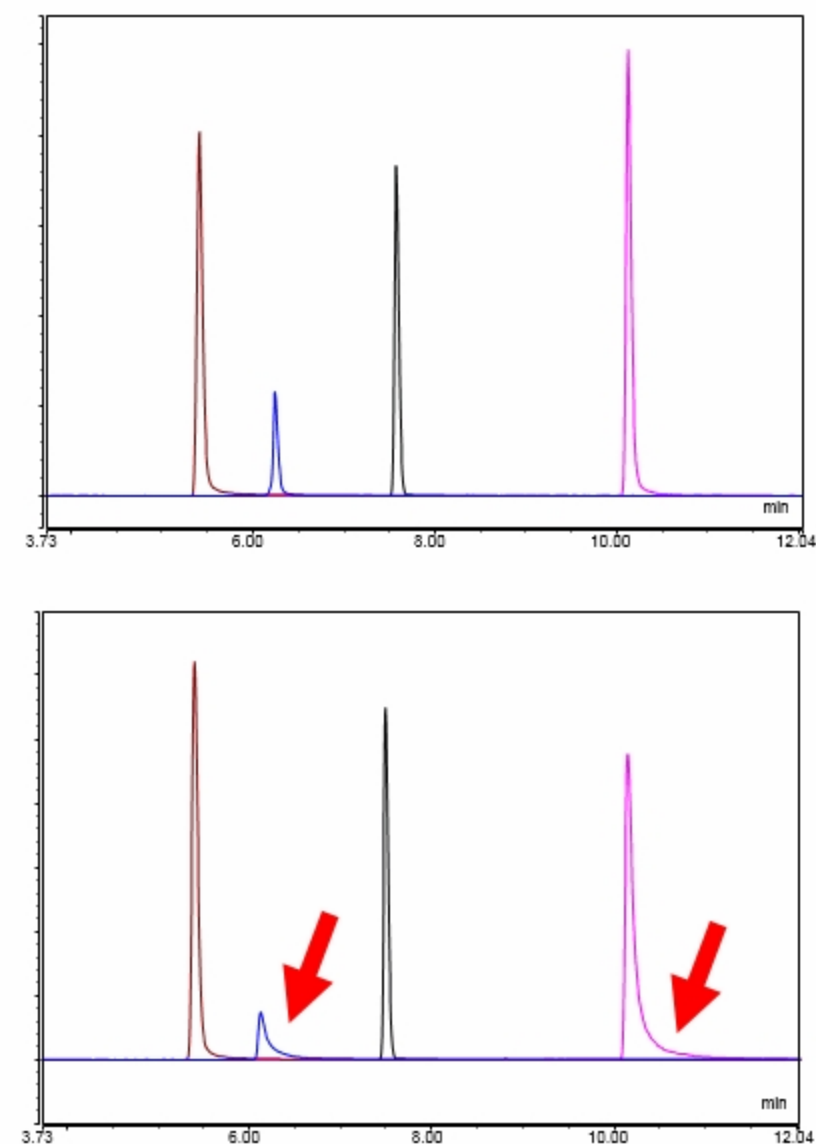
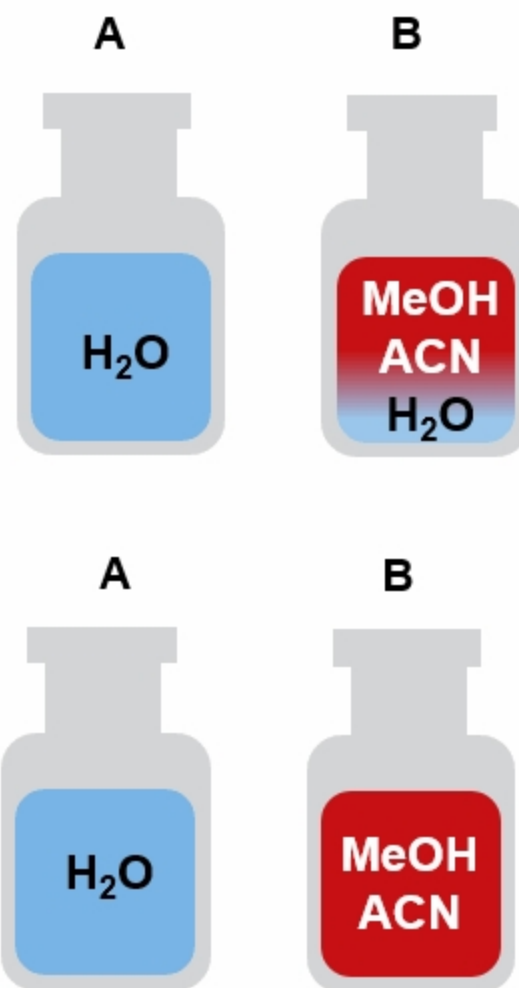
# Veterinary Drugs Analysis: Effect of Ti Corrosion

Aqueous eluent	0.05% formic acid
Organic eluent	MeOH / ACN +0.05% formic acid
Gradient	0 → 95% organic in 14 minutes

Polar embedded reversed phase

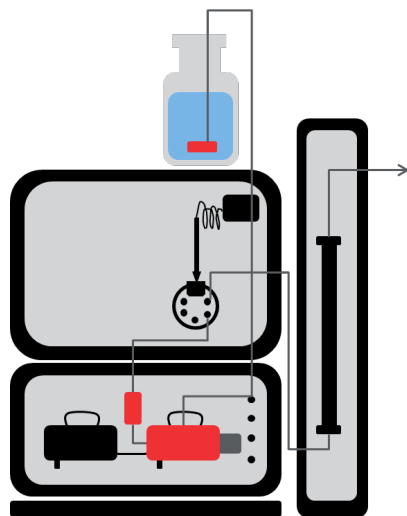
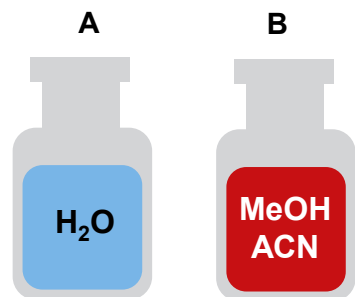


Tailing for some compounds when pump block B is pure organic



For research use only. Not for use in diagnostic procedures

# Ti Leaching from a Biocompatible System



- ICP-MS analysis of effluents collected w/o column: 2 ppb Ti
- All Ti fluidic components contribute to Ti leaching
- The solvent frits are most critical (very large surface)

How do Ti ions affect chromatography?

# Investigating the Mechanism: The Experiments



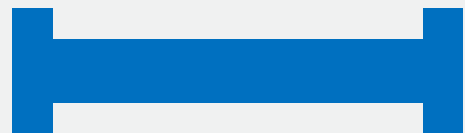
New column

Amide **polar embedded reversed phase**

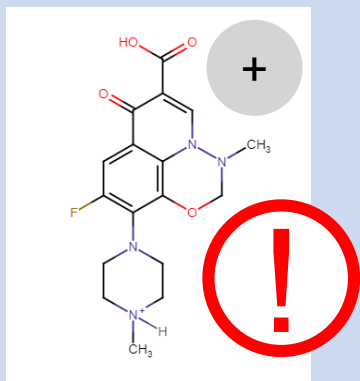
Thermo Scientific™ Acclaim™ PA2 RSLC (2.2  $\mu\text{m}$ , 2.1x150mm) column

Column contaminated by titanium

- High peak asymmetry
- Permanent change
- Ti is immobilized in the column

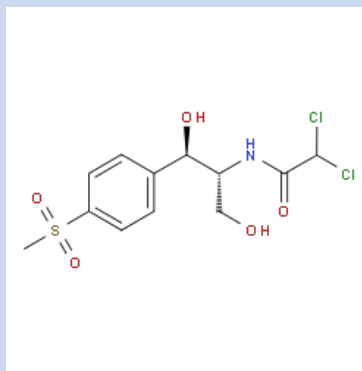


7 fluoroquinolones



Prone to tailing

thiamphenicol



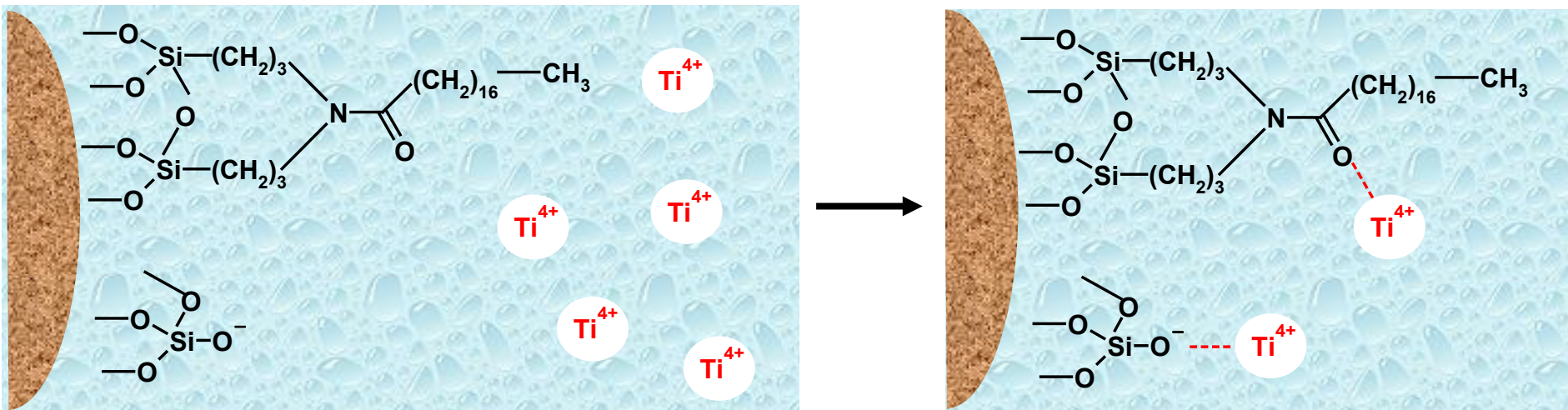
No tailing

- **ISOCRATIC** ( $\text{H}_2\text{O}$ , MeOH, ACN, formic acid) **pH 2.9**
- **Non-corrosive conditions**  
(Any part of fluidic always in contact with water)

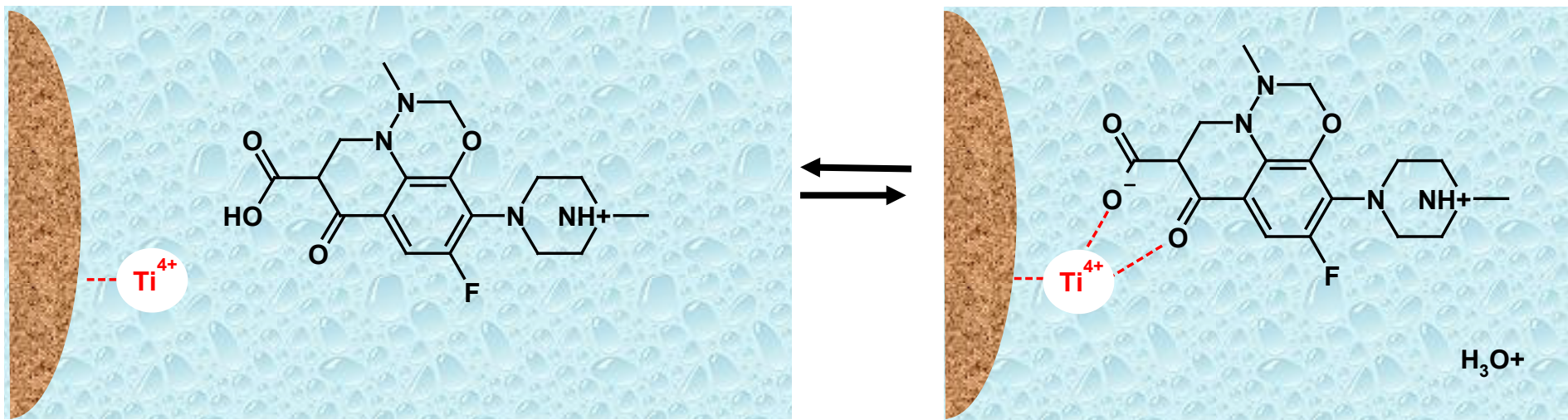


# Retention Mechanism Model with Leaching Titanium

## 1. Dissolved titanium binds to the stationary phase



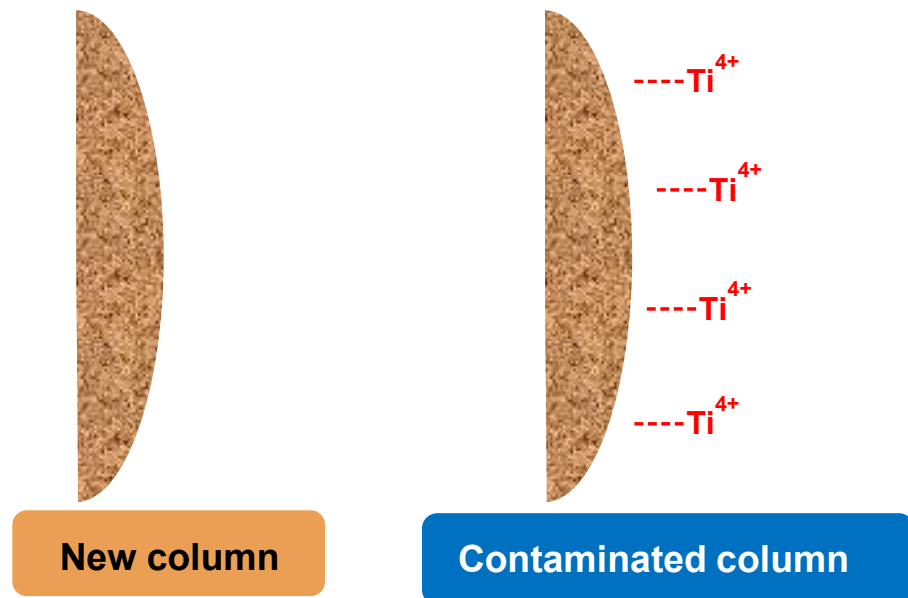
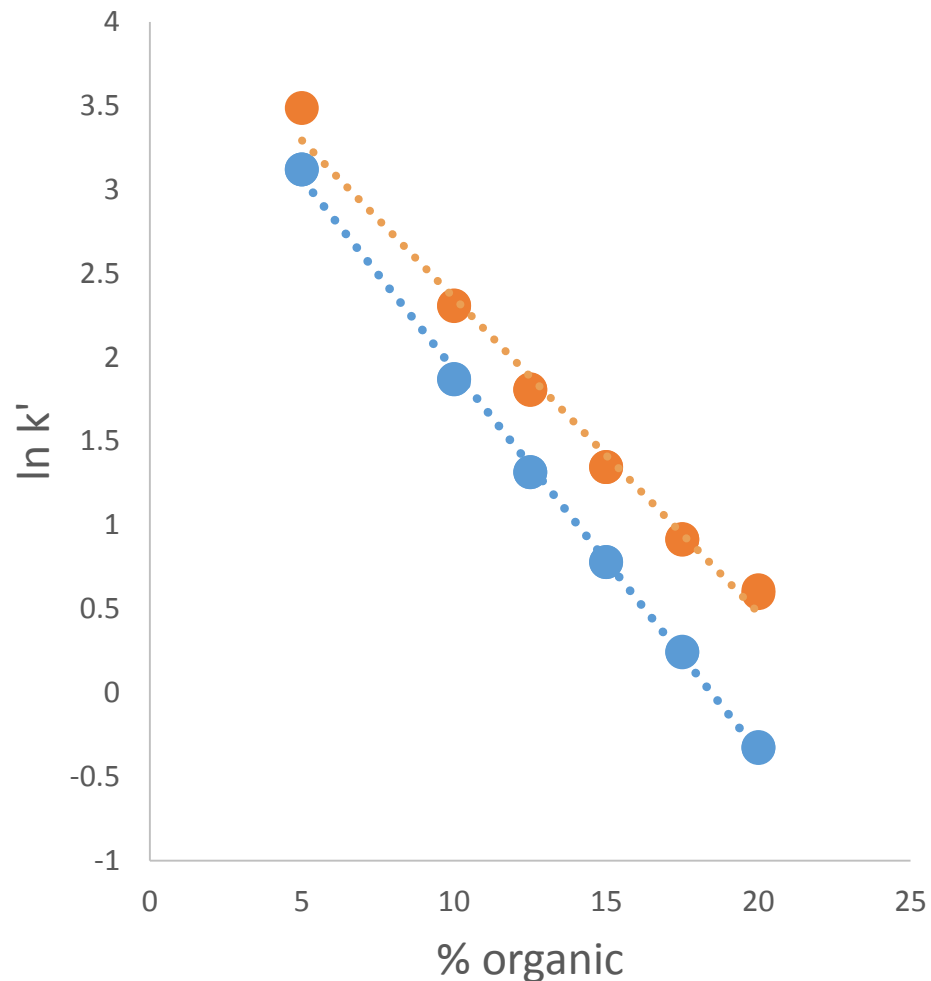
## 2. Complex formation\* of fluoroquinolones with immobilized titanium



\*Uivarosi V. *Molecules* 2013 “Metal complexes of quinolone antibiotics and their application”

# Influence of Organic Content on Retention

Ciprofloxacin



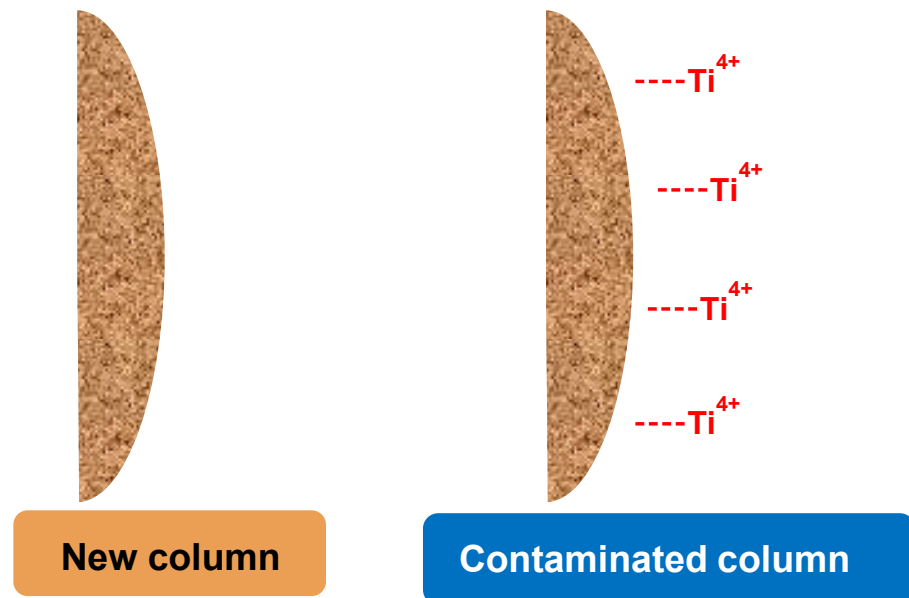
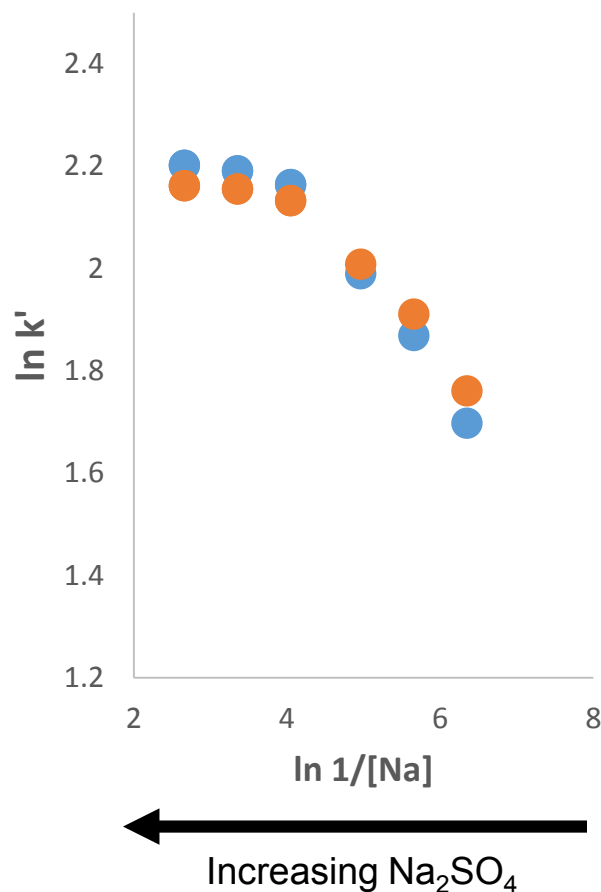
- Reversed phase is the main retention mechanism
- Ti cations make the contaminated column less hydrophobic

**However this does not explain the tailing**



# Influence of Salt Content on Retention

Ciprofloxacin

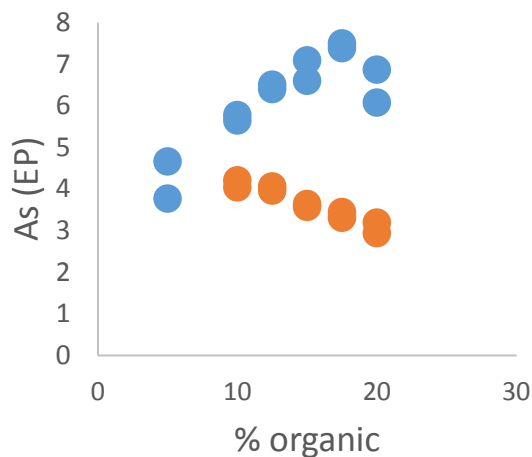


- Without salt - Contaminated column is much less retentive  
With salt - Column behavior becomes more similar
- Contribution of electrostatic repulsion to the mechanism (Retention increases with salt)

**However this does not explain the tailing**

# Influence of Organic Content on Peak Asymmetry

Ciprofloxacin



- Complex formation of fluoroquinolones with immobilized titanium
- complex stability is influenced by organic content
- Tailing is due to complex formation

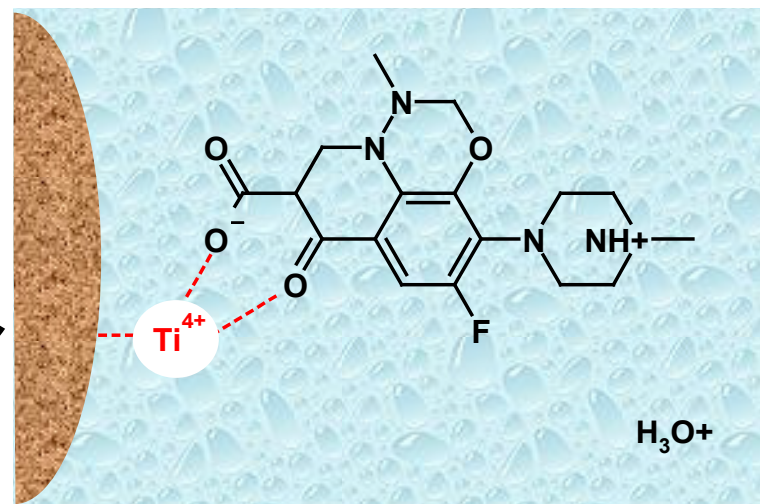
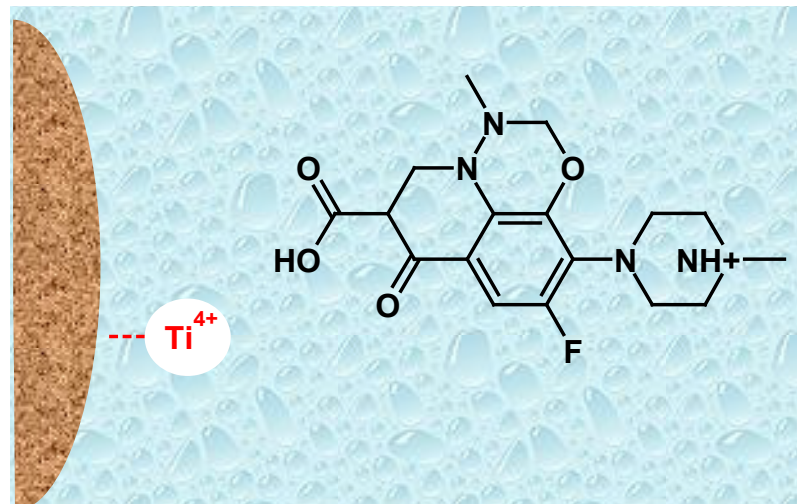
Increased complex stability  
organic 5-15%



organic 20%



Decreased fluoroquinolone acidity



# Conclusions

- Leaching of titanium from biocompatible systems observed when anhydrous methanol/acetonitrile was used as eluent.
- Peak shape of some drugs is strongly affected.
- Titanium ions are immobilized on the stationary phase and reduce column hydrophobicity.
- Fluoroquinolones form complexes with the immobilized titanium, creating a secondary interaction.
- Conventional C18 columns are not affected by titanium.

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