The Development of ZrO\textsubscript{2} Based HPLC: From Colloid to Column

Department of Chemistry
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Outline

• Colloid to particle.

• Stationary phase synthesis.
  • Polybutadiene-ZrO$_2$
  • Polystyrene -ZrO$_2$
  • P-EDTA/PBD -ZrO$_2$
  • Carbon Clad -ZrO$_2$

• Phase Properties.
  • Stability
  • Selectivity

• Network Polymer Silica Phases.
  • Acid stability
High pH Stability Comparison

**Exposure Conditions:** Mobile phase, ACN/50mM Potassium phosphate buffer at indicated pH; Temperature, 30 °C.

**LC Conditions:** Mobile phase, ACN (or THF)/50mM Potassium phosphate buffer at indicated pH; Flow Rate, 1.0 mL/min.; Temperature, 30 °C; Injection Volume, 5 uL; Detection, 254nm.
Methods of Making Spherical Particles from Colloids

Aqueous suspension of ceramic colloid

Spray drying

Droplets sprayed in air

Dried

Sintered

Polymerization

Water-soluble monomers added

Polymer precipitated (collecting colloid)

Washed, polymer burned, remaining ceramic sintered

Oil emulsion

Droplets emulsified in oil

Water extracted into oil, dried

Washed, sintered

Aqueous suspension of ceramic colloid
Polymerization-Induced Colloid Aggregation of Zirconia (PICA)

1000A sol
pH 1.5-1.8
20 wt% solids

urea (7.5 g/l sol)
formaldehyde
8:1 vol ratio
sol:formaldehyde

15-30 min.

Dilute and collect by filtration

175°C, 3 days, vacuum drying
375°C, 2h, air burn
Sinter and harden
750°C, 3h
900°C, 6h
SEM of Porous Zirconia

Particles are monodisperse and spherical as formed!
## Properties of PICA 7

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Property</th>
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<tbody>
<tr>
<td>Surface area (m²/g)</td>
<td>30</td>
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<tr>
<td>Pore volume (cc/g)</td>
<td>0.5</td>
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<tr>
<td>Pore diameter (Å)</td>
<td>250-300</td>
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<tr>
<td>Porosity</td>
<td>0.5</td>
</tr>
<tr>
<td>Density (gm/cc)</td>
<td>5.8</td>
</tr>
<tr>
<td>Particle diameter (µ)</td>
<td>2.5</td>
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</tbody>
</table>
Deposition of Polybutadiene (PBD)

- Suspend zirconia particles in hexane solution containing PBD and dicumyl peroxide.
- Sonicate the slurry with vacuum for 5 minutes.
- Rotate the slurry at 20 rpm for 2 hours.
- Remove hexane by vacuum at 36 °C.
- Cross-link PBD in vacuum oven at 160 °C for 4 hours.
- Extract particles with toluene for 12 hours.
Performance

Separation on PBD-Zirconia

1. Lidocaine
2. Norpseudoephedrine
3. Tryptamine
4. Quinidine
5. Amitriptyline
6. Nortriptyline

20% ACN, 20 mM ammonium phosphate, pH 7.5; 0.8 mL/min; 30 °C
Polystyrene-ZrO₂ Synthetic Strategy

Step 1. Synthesis of Copolymer (CMS/VMS)

Step 2. Adsorption of Copolymer

Step 3. Thermal Crosslinking

CMS/VMS-ZrO₂

PS-ZrO₂

160°C
Pore Size Distribution

**Nitrogen Porosimetry**

- Bare Zirconia
- PS-ZrO$_2$

**Size Exclusion Chromatography**

- *no significant change in pore size distribution.*
Nature of Zirconia’s Surface

Brönsted Acid: $\text{ZrOH} + \text{OH}^- \rightleftharpoons \text{ZrO}^\cdot + \text{H}_2\text{O}$

Brönsted Base: \[ \text{Zr} \overset{\cdot}{\overset{\cdot}{\overset{\cdot}{\overset{\cdot}{\text{O}}}}} \text{Zr} + \text{H}^+ \rightleftharpoons \text{Zr} \overset{\cdot}{\overset{\cdot}{\overset{\cdot}{\overset{\cdot}{\text{O}}}}} \text{Zr} \]

Lewis Acid: $\text{Zr(OH}_2\text{)} + \text{OOC—R} \rightleftharpoons \text{ZrOOC—R} + \text{H}_2\text{O}$
Acidic Analytes on PBD-ZrO$_2$

**Benzylalcohol**
- $k' = 0.66$
- $N = 1400$
- $A_s = 1.19$

**Phenylacetic Acid**
- $k' = 5.64$
- $N = 55$
- $A_s = 3.15$

Acidic Analytes: Long Retention and Low Efficiency

10% ACN, 0.3 M acetic acid, pH 2.4; 30 °C; 1 mL/min.
Effect of Eluent on Alkoxybenzoic Acids

40 mM Acetate pH 4

N = 260
A_s = 3.35

40 mM Phosphate pH 2.15

N = 3250
A_s = 1.07

25% ACN, 40 mM above additive, 5 mM NH_4F; 0.6 mL/min; 30 °C; 254 nm.
1. Coat bare zirconia with polybutadiene (PBD).
2. PBD Crosslinking using dicumyl peroxide as initiator.
3. Reflux PBD-ZrO$_2$ in Ethylenediamine N,N,N’,N’ tetra(methyleneephosphonic) acid (EDTPA) solution.
4. Wash to remove residual EDTPA.

Courtesy ZirChrom
**LC-MS Compatible Phase for Bases**

**Morphine**
M.W. 285.33

**Hydromorphone**
M.W. 285.33

**Codeine**
M.W. 299.36

**Hydrocodone**
M.W. 299.36

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**LC Conditions:** Column, 50 mm x 4.6 mm i.d. ZirChrom-EZ; Mobile phase, A = 20mM ammonium acetate, pH 6.0, B = ACN; Flow rate, 2.00 ml/min.; Temperature, 35 °C; Injection volume, 10 µl; Detection at 254 nm.; Solutes: 1=Morphine, 2=Hydromorphone, 3=Codeine, 4=Hydrocodone

**Courtesy ZirChrom**
**Column Efficiency**

**LC Conditions**: Column, 150 mm x 4.6 mm i.d. **ZirChrom-EZ**; Mobile phase, 35/65 ACN/Water; Temperature, 30 °C; Injection volume, 5 µl; Detection at 254 nm.; Solutes: 1=Acetone, 2=Phenol, 3=4-Chlorophenol, 4=Anisol, 5=Toluene

**Courtesy ZirChrom**
Carbon Coating of ZrO$_2$ by CVD

**Phase Synthesis**
- Place zirconia particles in reactor tube
- Heat reactor to 700°C
- Flow organic vapor over hot zirconia particles
- Soxhlet extract phase to remove soluble pyrolysis products

**Unique selectivity compared to bonded or polymer-coated phases**
Stereoisomer Separation on Carbon-Zirconia

(±)-Warfarin-(R)-MTPA ester
Non-electrolyte Probes

Nonpolar
- Benzene
- Toluene
- Ethylbenzene
- p-xylene
- Propylbenzene
- Butylbenzene

Polar
- Bromobenzene
- p-Dichlorobenzene
- Anisole
- Methylbenzoate
- Naphthalene
- Acetophenone
- Benzonitrile
- Nitrobenzene
- p-Nitrotoluene
- p-Nitrobenzyl Chloride
- Benzophenone

HB Donor
- Benzyl alcohol
- 3-Phenyl propanol
- N-Benzyl formamide
- Phenol
- p-Chlorophenol
Selectivity Comparison

Normalized Log $k'$ (k' solute/k' benzene)
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