Mesoporous Silica Nanoparticles as Complex Bioactive Delivery Vehicles

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Characteristics of mesoporous materials

- High surface area (over 1000 m$^2$/g)
- Large pore volumes
- Sharp pore size distributions
- Stable compositions (chemically and thermally)
- Properties that can be designed and modified—particle size, particle shape, and surface functionalization

<table>
<thead>
<tr>
<th>Material (IUPAC notation)</th>
<th>Pore Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>microporous</td>
<td>&lt;2 nm</td>
</tr>
<tr>
<td>mesoporous</td>
<td>2-50 nm</td>
</tr>
<tr>
<td>macroporous</td>
<td>&gt;50 nm</td>
</tr>
</tbody>
</table>

Published in Garcia-Bennett Nanomedicine 2011 6 (5): 867-877
Abridged History of Mesoporous Silica Nanoparticles (MSNs)


1998 D. Zhao et al. Science SBA-15 (Santa Barbara Amorphous)
MSNs—promise as drug deliverers

ISI web of science by the topic of “mesoporous silica” and “drug delivery”
Structural Variation of MSNs

- Rods with 3 nm wide helicoidal pores
- Spheres with 3 nm wide cubic pores
- Spheres with 4 nm wide hexagonal pores
- Hexagonal plates with 10 nm wide hexagonal pores

Mesoporous Silica Nanoparticles (MSNs) for Drug Delivery

Advantageous Functional Options

- Large payloads
- Multiple payloads
  - Diagnostic-Therapeutic
  - Drug A-Drug B
- Solubilization
- Targeting
- Triggering
- Mechanization
MSNs Carry Functional Cargo of Multiple Types

- Immobilized Enzyme
- Protected Fluorescence Agent
- Gene/Drug Delivery
- MRI Contrast Agent
- Site-Specific Targeting
- Selective Surface Functionalization

Source: Chem. Commun., 2011, 47, 9972-9985
Si-Han Wu, Yann Hung, Chung-Yuan Mou; “Mesoporous silica nanoparticles as nanocarriers.”
Controlled Cargo Release

Published in: Michael W. Ambrogio; Courtney R. Thomas; Yan-Li Zhao; Jeffrey I. Zink; J. Fraser Stoddart; Acc. Chem. Res. 2011, 44, 903-913.
Release Controlled by pH

Benzimidazole on MSN

Cyclodextrin cap Hoescht or Dox. cargo

pH drops within lysosomal compartment of cells
Nanoimpellers work by cis-trans isomerization of azobenzene.

Release Controlled by Irradiation

Campothecin (hydrophobic)
Release Controlled by Oscillating Magnetic Field

Cyclodextrin cap Rhod. or Dox. cargo

37% cell death w/Doxorubicin cargo
Release Controlled by Redox

50% cell death w/Methotrexate cargo
Stop and Go Checkpoints for Nanomedicine Design

Biocompatibility and Biotranslocation of MSNs

in vitro cellular uptake, intracellular translocation and cytotoxicity

in vivo biodistribution, biodegradation, excretion, and toxicity
Biolocalization of loaded MSNs
Endocytosis of a single mesoporous silica nanoparticle into a human lung cancer cell observed by differential interference contrast microscopy” Wei Sun et al. Analytical and Bioanalytical Chemistry (2008) 391:2119–2125
Trafficking of PEGylated MSNs varies by shape
Hemolysis by MSNs Up Close

A

B

C

Published in: Yannan Zhao; Xiaoxing Sun; Guannan Zhang; Brian G. Trewyn; Igor I. Slowing; Victor S.-Y. Lin; ACS Nano 5, 1366-1375.
Results

Different by 

Geometry, 

Porosity, 

Cell Type

Adapted with permission from Tian Yu et al. ACS Nano 2011, 5, 1366-1375. Copyright © 2011 American Chemical Society
Particle Aging Effects?

Adapted from: Yu-Shen Lin; Christy L. Haynes; J. Am. Chem. Soc. 2010, 132, 4834-4842. Copyright © 2010 American Chemical Society
PEGylation and Inhibition of Hemolysis

Qianjun He, Jiamin Zhang, Jianlin Shi, Ziyan Zhu, Linxia Zhang, Wenbo Bu, Limin Guo, Yu Chen; Biomaterials 2009, 31(6), 1085-1092. and “Nanomedicine(s) under the Microscope” by Ruth Duncan and Rogerio Gaspar; Molecular Pharmaceutics 2011 8 (6), 2101-2141.

**PEG drawbacks:**
- Side effects from increased exposure to normal tissues
- Increased diameter alters mobility
- Not biodegradable, potential intracellular accumulation or tubular reabsorption

**MSNs as complex bioactive delivery vehicles: much more to be learned.**