Development of wüstite nanoparticles as efficient ROS-inducing agents for cancer therapy

Zhongchao Yi

PI: Sheng Tong

F. Joseph Halcomb III, M.D. Department of Biomedical Engineering
zyi228@uky.edu

8/4/2022
Cancer therapy

The roles of intracellular reactive oxygen species (ROS) levels in cancer therapies. Either higher or lower ROS levels can reduce the survival of cancer cells via multiple pathways.

Fenton reaction

\[ \text{Fe}^{2+} + \text{H}_2\text{O}_2 \rightarrow \text{Fe}^{3+} + \text{OH}^- + \text{OH}^- \] \hspace{1cm} (1)

\[ \text{Fe}^{3+} + \text{H}_2\text{O}_2 \rightarrow \text{Fe}^{2+} + \text{OOH}^- + \text{H}^+ \] \hspace{1cm} (2)

Type of iron oxide:
1. Oxide of Fe\(^{2+}\)
   - FeO: iron(II) oxide, wüstite
   - FeO\(_2\): iron dioxide
2. Mixed oxides of Fe\(^{2+}\) and Fe\(^{3+}\)
   - Fe\(_3\)O\(_4\): iron(II, III) oxide magnetite
   - Fe\(_4\)O\(_5\), Fe\(_5\)O\(_6\)
1. Oxide of Fe\(^{2+}\)
   - Fe\(_2\)O\(_3\): iron(III) oxide
     - \(\alpha\)-Fe\(_2\)O\(_3\) - hematite
     - \(\beta\)-Fe\(_2\)O\(_3\)
     - \(\gamma\)-Fe\(_2\)O\(_3\) - maghemite
Iron oxide nanoparticles (different compositions)

15.5nm (±0.8) wüstite nanoparticles

15.1nm (±1.1) maghemite nanoparticles

15nm (±1.3) magnetite nanoparticles

The TEM image of iron oxide nanoparticles. The size of nanoparticles was measured with TEM images in image J (n > 1000).
XRD (Crystal Structure)

XRD patterns of iron oxide nanoparticles. The figure shows the XRD pattern of 15nm magnetite, maghemite, and wüstite nanoparticles.

<table>
<thead>
<tr>
<th></th>
<th>Lattice parameter (a)</th>
<th>Standard lattice parameter (a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>15 nm wüstite nanoparticles</td>
<td>4.278 nm</td>
<td>4.296 nm</td>
</tr>
<tr>
<td>15nm magnetite nanoparticles</td>
<td>8.368 nm</td>
<td>8.378 nm</td>
</tr>
<tr>
<td>15nm maghemite nanoparticles</td>
<td>8.331 nm</td>
<td>8.340 nm</td>
</tr>
</tbody>
</table>
SAED (Crystal Structure)

15nm magnetite nanoparticles

15nm wüstite nanoparticles

<table>
<thead>
<tr>
<th>Ring</th>
<th>1</th>
<th>2</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>d(Å)</td>
<td>2.94</td>
<td>2.53</td>
<td>1.47</td>
</tr>
<tr>
<td>Fe₃O₄</td>
<td>2.96</td>
<td>2.52</td>
<td>1.48</td>
</tr>
<tr>
<td>hkl</td>
<td>2 2 0</td>
<td>3 1 1</td>
<td>4 4 0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Ring</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>d(Å)</td>
<td>2.96</td>
<td>2.54</td>
<td>2.11</td>
<td>1.48</td>
</tr>
<tr>
<td>FeO</td>
<td>2.49</td>
<td>2.16</td>
<td>1.53</td>
<td></td>
</tr>
<tr>
<td>hkl</td>
<td>1 1 1</td>
<td>2 0 0</td>
<td>2 2 0</td>
<td></td>
</tr>
</tbody>
</table>

**SAED patterns of iron oxide nanoparticles.** The figure shows the SAED pattern of 15nm synthesized magnetite and wüstite nanoparticles.
HRTEM image of 15 nm wüstite nanoparticles. It is difficult to calculate lattice parameters due to low resolution.
Dependence of catalytic activity on the size and composition of nanoparticles

**Michaelis–Menten curves for IONPs.** (A) Wüstite nanoparticles have higher catalytic activity. (B) The ROS generation increased as the size of nanoparticles decreases.
Conclusions

1. We have developed methods for synthesizing wüstite, magnetite, and maghemite nanoparticles of different sizes.

2. Compared with magnetite and maghemite nanoparticles, **wüstite nanoparticles** have higher catalytic activity. As the wüstite particles' size decreases, the catalytic activity will be increased.

EM methods used

1. TEM → size

2. XRD and SAED → composition
Acknowledge

Tong lab:
Dr. Xiaoyue Yang

Chapelin lab:
Dr. Fanny Chapelin

Funding:
• KY-INBRE grant (P20GM103436)
• NIH/NIBIB R01 (R01EB026893)
• NIGMS/COBRE pilot grant (P20GM121327)