Fluorescent Magnetic Nanoparticles for Biomedical Applications

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Aim and Motivations

In recent years, bifunctional probes with both magnetic and fluorescent properties have received a lot of attention for both in vivo and in vitro biomedical and biotechnological applications [1-2]. In this thesis, the main goal was to synthesize and to characterize novel magnetic fluorescent nanoparticles. These nanoparticles (NPs) involve superparamagnetic iron oxide nanoparticles (SPIONS), a fluorescently-labeled polymer absorbed onto the iron oxide surface encapsulated within a silica shell. Four different percentages of fluorescently-labeled polymers were tested. Then surface amino groups were introduced by a silanization reaction involving 3-aminopropyl triethoxysilane (APTES) followed by a PEGylation step. Therefore three different kinds of fluorescent nanoparticles were obtained with positive, negative and neutral surfaces. The cytotoxicity and the internalization of the NPs were assayed on two different cell lines, HeLa cells and RAW 264.7 macrophages.

Methods

• Step 1: Preparation of FITC labeled amine-PVA
• Step 2: SPIONS synthesis by co-precipitation of Fe3+/Fe2+ salts solutions, followed by an oxidation reaction
• Step 3: PVA-SPIONS
• Step 4: Silica encapsulation
• Step 5: Surface functionalization with APTES
• Step 6: PEGylation

Characterization

<table>
<thead>
<tr>
<th>Samples</th>
<th>Size TEM [nm]</th>
<th>Hydrodynamic Diameter [nm]</th>
<th>Zeta potential [mV at pH 7.4]</th>
</tr>
</thead>
<tbody>
<tr>
<td>SPIONS@SiO2 0%</td>
<td>44 ± 11</td>
<td>114 ± 33</td>
<td>-36.7 ± 0.7</td>
</tr>
<tr>
<td>SPIONS@SiO2 1%</td>
<td>40 ± 9</td>
<td>123 ± 12</td>
<td>-30.8 ± 1.2</td>
</tr>
<tr>
<td>SPIONS@SiO2 5%</td>
<td>41 ± 9</td>
<td>122 ± 22</td>
<td>-30.5 ± 1.1</td>
</tr>
<tr>
<td>SPIONS@SiO2 10%</td>
<td>42 ± 9</td>
<td>137 ± 8</td>
<td>-30.8 ± 1.2</td>
</tr>
<tr>
<td>SPIONS@SiO2 25%</td>
<td>37 ± 9</td>
<td>116 ± 11</td>
<td>-23.6 ± 1.5</td>
</tr>
</tbody>
</table>

Typical composition of SPIONS@SiO2 (in mass): 1% γ-Fe2O3, 1% Polymer, 98% SiO2.

In vitro studies

• Internalization in RAW 264.7 macrophages

Cytotoxicity was assayed by MTS assay. The fluorescent magnetic NPs did not show any toxicity towards HeLa cells. A slight decrease of cell viability can be noticed in macrophages incubated with positive NPs, which could be due to a higher internalization of these NPs.

• Cellular iron

Cells were incubated for 24h with SPIONS@SiO2. Cellular iron was determined by measuring the iron susceptibility of the cells and by using a calibration curve. HeLa cells incubated with 56 μg Fe/ml contained the highest amount of iron. Macrophages showed lower values but it is possibly due to the inefficient harvest of these cells.

Summary

The synthesized fluorescent magnetic nanoparticles:
• have different surface charges: positive, neutral and negative, confirming the efficient surface functionalization and PEGylation steps.
• have a hydrodynamic diameter from 115 nm to 250 nm.
• show no toxicity toward HeLa and macrophages cells at a maximum iron concentration of 56 μg/ml.
• are internalized by HeLa cells and macrophages with the exception of PEGylated NPs.

References


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Nanoscale Research Letters