Solid and Solution NMR Characterisation of Modified Dextrans for Drug Delivery

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Background
The safe and effective delivery of drugs (e.g., anticancer drugs) is a significant challenge for many reasons – drugs are often poorly soluble; harsh environments in the body can damage drugs before they reach the target area; drugs can be cleared by the body’s defence mechanisms; and the lack of selectivity can cause reduced concentrations at the diseased sites and cause potentially severe side effects. Many of these problems can be overcome by the use of well-designed polymeric drug carriers. Desirable characteristics include the use of biodegradable polymers; stimuli-sensitive systems to release the drug preferentially at targeted sites; and nanosized carriers to take advantage of passive targeting via the enhanced permeation and retention effect. This study aimed to make a biodegradable, pH-sensitive polymer based on dextran which would self-assemble into nanocapsules in water for the delivery of anticancer drugs eg. doxorubicin.

Synthesis

Acetalated Dextran
Solid state NMR

Acetalated dextran is a relatively new material for drug delivery, and so few methods exist to determine important characteristics. We have applied both solid state and solution NMR to determine the following:

- Degree of substitution (DS) – the number of substituents per 100 repeating units
- Ratio of acyclic to cyclic acetals
- % Hydroxyl coverage
- Number of acetals and free hydroxyls per chain (62 repeating units per 10,000 g mol⁻¹ chain)
- Molecular weight
- Substitution patterns (?)

<table>
<thead>
<tr>
<th></th>
<th>DS acyclic</th>
<th>DS cyclic</th>
<th>Ratio acyclic : cyclic</th>
<th>OH coverage</th>
<th>No. acyclic per chain</th>
<th>No. cyclic per chain</th>
<th>No. free OH per chain</th>
<th>Molecular weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ac-Dextran-POEGMEMA</td>
<td>40</td>
<td>93</td>
<td>1.23</td>
<td>75%</td>
<td>23</td>
<td>58</td>
<td>40</td>
<td>14,100 g mol⁻¹</td>
</tr>
</tbody>
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Solution NMR

Ac-Dextran macroRAFT

Ac-Dextran-POEGMEMA

Solution HSQC-ed, 308 K in dmso-d⁶