A Bioadhesive Nanoplatform Enhances the Permeation of Drugs Used to Treat Diabetic Macular Edema

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Results

Synthesis and Characterization of Block and Random Glycopolymers

The $^1$H NMR spectra of AAPBA and AGA were shown in Figure S1. The monomers of AAPBA and AGA as well as the RAFT chain transfer agent, CPADB were synthesized according to the earlier reported method\cite{1-3}. As shown in Scheme S1, a series of block copolymer p(AAPBA-\textit{b}-AGA) and random copolymer p(AAPBA-\textit{r}-AGA) with different composition ratios were obtained via RAFT polymerization by varying the molar ratio of monomers to the corresponding RAFT chain transfer agent. Copolymer structures were confirmed by $^1$H NMR spectroscopy as shown in Figure S2. Compared with the spectra of AAPBA and AGA, signals of double bond in p(AAPBA-\textit{b}-AGA) and p(AAPBA-\textit{r}-AGA) completely disappeared. On the contrary, peaks of phenyl group at 6.7–7.8 ppm and signals of sugar residue at 3.0–3.8 ppm in sugar residue were retained. Furthermore, the new resonance signals in the ranges of 0.9–2.3 appeared in the spectrum of p(AAPBA-\textit{b}-AGA) or p(AAPBA-\textit{r}-AGA), which were assigned to protons from main chain. These results indicated that both block copolymer p(AAPBA-\textit{b}-AGA) and random copolymer p(AAPBA-\textit{r}-AGA) were synthesized successfully. The features of peaks from sugar in the copolymers. The composition ratio of AAPBA and AGA in the copolymer was also calculated using $^1$H NMR integral intensity of signals between the 4H in phenyl moiety and 5H in sugar moieties and the results are shown in Table S1. The integral calculation results are consistent with the feed ratio, and the corresponding block copolymer has a similar composition ratio with the random copolymer.
The FT-IR spectroscopy was further performed to analyze the construction composition of phenylboronic acid -based glycopolymers. As shown in Figure S3, the spectra of p(AAPBA-\textit{b}-AGA) and p(AAPBA-\textit{r}-AGA) exhibit a broad absorption band with a range of 3200 to 3600 cm\(^{-1}\), which was assigned to the hydrogen bonds formed between the hydroxyls in phenylboronic acid groups and carbohydrate moieties. The absorption band peaks at 3272 cm\(^{-1}\), which was due to N-H stretching. The amide I band assigned to C=O stretching resulted in an absorption band of 1650 cm\(^{-1}\), while an absorption band at 1548 cm\(^{-1}\) was attributed to the N-H bending vibration (amide II band) of a secondary amide. The typical absorption bands of phenyl ring in pAAPBA from 1500 to 1350 cm\(^{-1}\) region and absorption peaks at 797 and 711 cm\(^{-1}\) were observed. In addition, the band in the 1080-1200 cm\(^{-1}\) region resulted from the C-O stretching and corresponded to the alkoxy bond in the carbohydrate moieties. There is no difference between the FT-IR spectra of p(AAPBA-\textit{b}-AGA) and p(AAPBA-\textit{r}-AGA). These results revealed the successful preparation of block and random copolymers.

\begin{figure}
\centering
\includegraphics[width=\textwidth]{scheme.png}
\caption{Scheme S1. Synthesis of (A) random and (B) block glycopolymers.}
\end{figure}
Figure S1. $^1$H NMR spectra of (A) AAPBA and (B) AGA.

Figure S2. $^1$H NMR spectra of (A) p(AAPBA$_{45}$-$b$-AGA$_{15}$)/p(AAPBA$_{45}$-$r$-AGA$_{15}$) and (B) p(AAPBA$_{30}$-$b$-AGA$_{30}$)/p(AAPBA$_{30}$-$r$-AGA$_{30}$).

Figure S3. FT-IR spectra of pAAPBA, p(AAPBA-$b$-AGA), and p(AAPBA-$r$-AGA).
### Table S1. Constitution of Amphiphilic Glycopolymers

<table>
<thead>
<tr>
<th>Sample</th>
<th>Monomer</th>
<th>RAFT agent</th>
<th>Conv (wt %)&lt;sup&gt;b&lt;/sup&gt;</th>
<th>AAPBA/AGA</th>
<th>Theory&lt;sup&gt;a&lt;/sup&gt;</th>
<th>&lt;sup&gt;1&lt;/sup&gt;H NMR&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>p(AAPBA&lt;sub&gt;45&lt;/sub&gt;-b-AGA&lt;sub&gt;15&lt;/sub&gt;)</td>
<td>AGA</td>
<td>-</td>
<td>pAAPBA&lt;sub&gt;45&lt;/sub&gt;</td>
<td>80.4</td>
<td>3</td>
<td>3.12</td>
</tr>
<tr>
<td>p(AAPBA&lt;sub&gt;30&lt;/sub&gt;-b-AGA&lt;sub&gt;30&lt;/sub&gt;)</td>
<td>AGA</td>
<td>-</td>
<td>pAAPBA&lt;sub&gt;30&lt;/sub&gt;</td>
<td>60.7</td>
<td>1</td>
<td>0.75</td>
</tr>
<tr>
<td>p(AAPBA&lt;sub&gt;45&lt;/sub&gt;-r-AGA&lt;sub&gt;15&lt;/sub&gt;)</td>
<td>AGA</td>
<td>AAPBA</td>
<td>CPADB</td>
<td>78.2</td>
<td>3</td>
<td>3.03</td>
</tr>
<tr>
<td>p(AAPBA&lt;sub&gt;30&lt;/sub&gt;-r-AGA&lt;sub&gt;30&lt;/sub&gt;)</td>
<td>AGA</td>
<td>AAPBA</td>
<td>CPADB</td>
<td>91.9</td>
<td>1</td>
<td>0.91</td>
</tr>
</tbody>
</table>

<sup>a</sup>The theoretical molar ratio of AAPBA/AGA;  
<sup>b</sup>The approximate polymerization conversion and copolymer compositions were measured on the basis of the integral intensity of the <sup>1</sup>H NMR spectra.

### Colloidal Stability of PBA-GC NPs

**Figure S4.** Colloidal stability of (A) PBA-GC-b<sub>1</sub> NPs, (B) PBA-GC-b<sub>2</sub> NPs, (C) PBA-GC-r<sub>1</sub> NPs, and (D) PBA-GC-r<sub>2</sub> NPs.
TEM Micrographs of PBA-GC@DEX NPs

Figure S5. TEM micrographs of PBA-GC@DEX NPs and size distribution determined by DLS. (A: PBA-GC-b@DEX NPs; B: PBA-GC-r@DEX NPs).

REFERENCES

