Electronic Supplementary Information

Controlled release of lidocaine hydrochloride from polymerized drug-based deep-eutectic solvents

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FIGURE S1. DSC of the drug-based deep-eutectic solvents.
FIGURE S2. Analysis of carbonyl in acrylic acid (A), methacrylic acid (B), and AALidHCl (C) and MAALidHCl (D) DES.

Bonded carbonyl fraction calculated for monomers and DESs from FTIR analysis.

<table>
<thead>
<tr>
<th></th>
<th>Peak wavenumber (cm⁻¹)</th>
<th>Peak area</th>
<th>$X_{C=O \text{ bonded}}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>AA</td>
<td>1695</td>
<td>3122.94</td>
<td>0.78</td>
</tr>
<tr>
<td></td>
<td>1730</td>
<td>712.14</td>
<td></td>
</tr>
<tr>
<td>AA-LidHCl</td>
<td>1688</td>
<td>2863.30</td>
<td>0.87</td>
</tr>
<tr>
<td></td>
<td>1724</td>
<td>350.40</td>
<td></td>
</tr>
<tr>
<td>MAA</td>
<td>1690</td>
<td>2243.43</td>
<td>0.86</td>
</tr>
<tr>
<td></td>
<td>1731</td>
<td>313.35</td>
<td></td>
</tr>
<tr>
<td>MAA-LidHCl</td>
<td>1689</td>
<td>1336.33</td>
<td>0.57</td>
</tr>
<tr>
<td></td>
<td>1715</td>
<td>838.41</td>
<td></td>
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</tbody>
</table>
The bonded carbonyl fraction for monomers and eutectic mixtures was calculated using the following expression [1]:

\[ X_{\text{bonded} \ C = O} = \frac{1}{1 + 1.2 \frac{A_{\text{free} \ C = O}}{A_{\text{bonded} \ C = O}}} \]

*A Voigt model was used to fit the spectra.


**FIGURE S3.** \(^1\)H NMR of AA-LidHCl and MAA-LidHCl DESs.

AA-LidHCl DES (molar ratio 3 : 1) in CDCl\(_3\)

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<table>
<thead>
<tr>
<th>SAMPLE</th>
<th>(\delta) (ppm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>AA</td>
</tr>
<tr>
<td></td>
<td>H – C – H = C – H – COOH</td>
</tr>
<tr>
<td>LidHCl*</td>
<td>2.12 7.19 9.15 3.22 7.0 3.37 1.56</td>
</tr>
<tr>
<td>AA*</td>
<td>6.52 5.96 6.14 12.0</td>
</tr>
<tr>
<td>AA-LidHCl 3 : 1</td>
<td>6.50 6.10 6.29 2.32 7.20 10.2 4.58 9.09 3.36 1.36</td>
</tr>
</tbody>
</table>
MAA-LidHCl DES (molar ratio 3 : 1) in CDCl$_3$

![NMR Spectrum of MAA-LidHCl DES](image)

<table>
<thead>
<tr>
<th>SAMPLE</th>
<th>MAA</th>
<th>LidHCl·H$_2$O</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAA*</td>
<td>6.26 5.68 1.96</td>
<td>2.12 7.19 9.15 3.22 7.0 3.37 1.56</td>
</tr>
<tr>
<td>MAA-LidHCl 3:1</td>
<td>6.21 5.69 1.96</td>
<td>1.29 7.09 10.5 4.58 9.18 3.31 1.29</td>
</tr>
</tbody>
</table>

*Data from SDBSWeb: http://riodb01.ibase.aist.go.jp/sdbs/ (National Institute of Advanced Industrial Science and Technology, 08.15.2014)

**Data from ChemDraw™ $^1$H NMR estimation.

FIGURE S4. Photograph of the polymer-drug monoliths.
**FIGURE S5.** Thermogravimetric analysis of the polyacrylates-lidocaine hydrochloride and lidocaine hydrochloride monohydrate.

![Thermogravimetric analysis graphs](image)

**FIGURE S6.** $^1$H NMR of pure lidocaine hydrochloride monohydrate (A), lidocaine hydrochloride released in D$_2$O from PAA-LidHCl (B) and PMAA-LidHCl (C) and P(AA-co-MAA)-LidHCl.

![NMR spectra](image)
FIGURE S7. % Cumulative release of LidHCl versus the square root of time and linear fitting to Fickian model with $n=0.5$. 

- **PAA pH 7 0.5M**
  - $y = 25.962x - 2.5169$
  - $R^2 = 0.9924$
  - PAA pH 7 0.5M
  - Linear (PAA pH 7 0.5M)

- **PAA pH 7 0.1M**
  - $y = 22.701x + 3.6498$
  - $R^2 = 0.9852$
  - PAA pH 7 0.1M
  - Linear (PAA pH 7 0.1M)

- **PAA pH 6 0.5M**
  - $y = 26.595x + 2.7718$
  - $R^2 = 0.9857$
  - PAA pH 6 0.5M
  - Linear (PAA pH 6 0.5M)

- **PAA pH 6 0.1M**
  - $y = 33.413x + 2.9265$
  - $R^2 = 0.983$
  - PAA pH 6 0.1M
  - Linear (PAA pH 6 0.1M)

- **PMMA pH 7 0.5M**
  - $y = 32.071x - 4.6412$
  - $R^2 = 0.9683$
  - PMMA pH 7 0.5M
  - Linear (PMMA pH 7 0.5M)

- **PMMA pH 7 0.1M**
  - $y = 28.253x + 4.395$
  - $R^2 = 0.9815$
  - PMMA pH 7 0.1M
  - Linear (PMMA pH 7 0.1M)

- **PMMA pH 6 0.5M**
  - $y = 16.329x - 1.3762$
  - $R^2 = 0.9902$
  - PMMA pH 6 0.5M
  - Linear (PMMA pH 6 0.5M)

- **PMMA pH 7 0.1M**
  - $y = 22.483x + 0.9452$
  - $R^2 = 0.9938$
  - PMMA pH 7 0.1M
  - Linear (PMMA pH 7 0.1M)
FIGURE S8. Diameter of PAA-LidHCl cylinders at pH 6 (A) and pH 7 (B) versus the square root of time and linear fitting to Fickian model with n=0.5.

FIGURE S9. Experimental setup for frontal polymerization.

FIGURE S10. Calibration curve for the quantification of LidHCl by UV-Vis spectroscopy at 263 nm.