Implantable and Injectable Depot System for Sustained Release of Lidocaine to Address Post-operative Pain

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Background
Arthroplasty surgeries are associated with post-operative pain and significant resource consumption. Effective control of post-operative pain correlates with improved functional recovery, reduced complications, reduced hospital stay and reduced healthcare costs. Local anaesthetics such as lidocaine, have been found effective in treating post-operative pain (1). However the short duration of action of lidocaine requires frequent administration.

Aim
To deliver lidocaine to local tissues over an extended period of time following joint surgeries using biodegradable materials.

In-situ Gel Preparation
In-situ gelling depot systems were investigated to achieve the sustained delivery of lidocaine. A lidocaine loaded, in-situ gelling depot system was prepared by the cold method using the appropriate weight percentage of poloxamers (2), Polymer additives such as, polyvinyl pyrrolidone (PVP), hydroxypropyl methyl cellulose (HPMC) and carbopol were investigated to further sustain the drug release.

Results and Discussion

Table 1: Percentage of poloxamers, lidocaine and polymer additives (% w/w) used in different formulations. Sol-to-gel transition temperature of each formulation is also given as determined by the tube inversion method.

<table>
<thead>
<tr>
<th>Composition</th>
<th>F4</th>
<th>F4+PVP</th>
<th>F4+HPMC</th>
<th>F4+Carbopol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poloxamer407</td>
<td>17</td>
<td>17</td>
<td>17</td>
<td>17</td>
</tr>
<tr>
<td>Poloxamer188</td>
<td>14</td>
<td>14</td>
<td>14</td>
<td>14</td>
</tr>
<tr>
<td>Lidocaine</td>
<td>1.5</td>
<td>1.5</td>
<td>1.5</td>
<td>1.5</td>
</tr>
<tr>
<td>Water</td>
<td>67.5</td>
<td>67.2</td>
<td>67.2</td>
<td>67.4</td>
</tr>
<tr>
<td>Polymer additive</td>
<td>0</td>
<td>0.3</td>
<td>0.3</td>
<td>0.1</td>
</tr>
<tr>
<td>Sol-to-gel transition temperature (°C)</td>
<td>28.3±0.6</td>
<td>26.3±0.5</td>
<td>26.6±1.1</td>
<td>27.1±1.0</td>
</tr>
</tbody>
</table>

Figure 2. Cumulative release of lidocaine from different formulations. With the addition of polymer additives further reduction in the initial burst release was observed. Formulation with PVP (F4+PVP) demonstrated the lowest burst release, releasing 32.26 ± 1.82% of drug in first 6 h followed with steadily increase in release, 54.8 ± 1.4% released in 24 h, 85.3 ± 1.3% released in 48 h. Error bars represent standard deviation (n = 3).

Figure 3. Comparative cumulative release of lidocaine from F4+PVP formulation in intra-articular fluid (IAF) demonstrated faster release into ex-vivo than PBS (pH 7.4). Error bars represent standard deviation (n = 3).

Figure 3. The gelling behaviour of the selected formulation was investigated in human fresh-frozen cadaver knees (under the acquisition of Human Tissue Act (NZ 2008)). MRI Scans were performed pre-injection, post-injection and following physical actuation of the knee joint. The images viewed in all 3 planes show the gel (white in the images) to have spread comprehensively throughout the knee joint.

Conclusion
The study demonstrated that injectable depot systems are ideal platforms to achieve sustained drug delivery of lidocaine and can be used to treat post-operative pain.

Reference:

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