The aim of this work is to develop advanced multifunctional wound dressings for local delivery of an analgesic drug that can help to manage pain associated with chronic leg ulcers in older adults. Wafers with different compositions of carrageenan (CARR) Hyaluronan (HA), and lidocaine (LID) was proposed to obtain a system with analgesic properties and able to promote the wound healing process.

**MATERIALS**

- **k-Carrageenan**
  - Linear sulphated polysaccharides extracted from red edible seaweed
  - Widely used in the food industry for their gelling, thickening, and stabilizing properties
  - Used in pharmaceuticals as inactive excipient in pills/tablets
  - GRAS substance

- **Hyaluronic Acid**
  - Principal component of the human connective tissues
  - Direct action on tissue repair processes, including wound healing
  - Already used in industrial production of advanced dressing

- **Lidocaine**
  - Rapid onset of action and intermediate duration of efficacy
  - Widely employed to relieve itching, burning, and pain from skin inflammations, injected as a dental anaesthetic
  - Already used as local anaesthetic in wound healing

**WAFERS PREPARATION**

- **Freeze drying cycle**
  - Sample | CARR (% w/w) | HA (% w/w) | LID Loading (%) |
  - CARR | 100 | - | 10 |
  - CARR/HA<sub>50</sub> | 50 | 50 | 10 |
  - CARR/HA<sub>70</sub> | 70 | 30 | 10 |
  - CARR/HA<sub>90</sub> | 90 | 10 | 10 |

  - *All gel formulations are at 2% w/v*

- **Wafer composition**
  - CARR/HA composite wafers

  - *Wafers with different shapes and sizes can be prepared by freeze drying*
  - CARR/HA wafers can be easily loaded with LID
  - LID does not influence formulation process and final wafers

**WAFERS CHARACTERIZATION**

- **Scanning electron microscopy**
- **Some properties of the wafers**
  - Density (mg/cm³)
  - Water absorption (%) (Mean ± s.d.)
  - Water retention (%) (Mean ± s.d.)
  - EWC (%) (Mean ± s.d.)

<table>
<thead>
<tr>
<th></th>
<th>Density</th>
<th>Water absorption</th>
<th>Water retention</th>
<th>EWC</th>
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</thead>
<tbody>
<tr>
<td>CARR</td>
<td>0.25 ± 0.03</td>
<td>38.78 ± 1.51</td>
<td>87.3 ± 1.8</td>
<td>97.49 ± 0.99</td>
</tr>
<tr>
<td>CARR/HA&lt;sub&gt;50&lt;/sub&gt;</td>
<td>0.20 ± 0.02</td>
<td>30.32 ± 1.25</td>
<td>78.8 ± 4.1</td>
<td>97.33 ± 0.53</td>
</tr>
<tr>
<td>CARR/HA&lt;sub&gt;70&lt;/sub&gt;</td>
<td>0.35 ± 0.35</td>
<td>28.69 ± 1.75</td>
<td>77.1 ± 2.4</td>
<td>97.06 ± 0.21</td>
</tr>
<tr>
<td>CARR/HA&lt;sub&gt;90&lt;/sub&gt;</td>
<td>0.06 ± 0.06</td>
<td>26.55 ± 0.66</td>
<td>76.3 ± 1.1</td>
<td>97.30 ± 0.88</td>
</tr>
</tbody>
</table>

- **Wafers hardness**

  - *Increase in resistance to compressive deformation with increasing concentration of HA*
  - *More rigid wafers in presence of HA*

- **Water uptake**

  - Materials of known weight were placed on a new filter into a customized release apparatus and stored in a desiccator at 27 ± 3 °C for 7 days. The % uptake was calculated using the following equation:

  \[
  \text{% Uptake} = \left( \frac{W_1 - W_0}{W_0} \right) \times 100
  \]

  where W<sub>0</sub> and W<sub>1</sub> represent the weight of the hydrogels before and after the experiment.

- **Lidocaine release**

  - The presence of HA within the wafers decreases water uptake.

  - Wafers seems to be a very promising system for delivery of analgesic drug to the wound. Further studies are in progress to evaluate in vitro activity of the dressings and role of HA in the wound healing process.

- **The presence of HA within the wafers decreases water uptake**

- **Drug release driven by water uptake**

  - Controlled Lid release over 6 hours
  - Drug release driven by water uptake

- **Resistance to compression**

  - Critical parameters for handling properties
  - HA causes an increase in resistance to compressive deformation
  - A compression recovery table further from one indicate a permanent deformation of the wafers with a possible modification of internal structure