DEVELOPMENT OF ADVANCED ANALGESIC DRESSINGS FOR CHRONIC WOUND HEALING

UKICRS

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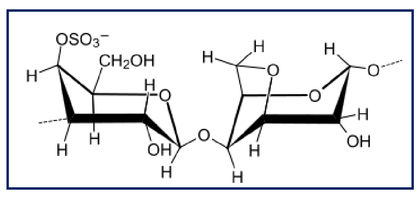
The aim of this work is to develop advanced multifunctional wound dressings for local delivery of an analgesic drug that can help to manage pain associated with chronic leg ulcers in older adults. Wafers with different compositions of carrageenan (CARR) Hyaluronan (HA), and lidocaine (LID) was proposed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

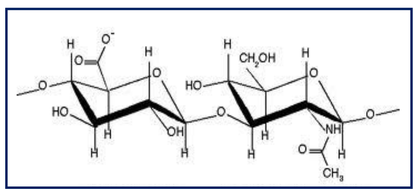
MATERIALS

κ-Carrageenan



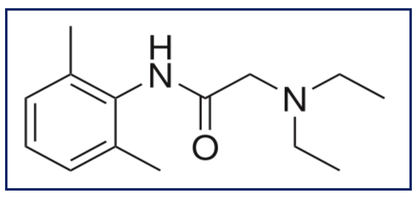
- ✓ Linear sulphated polysaccharides extracted from red edible seaweeds
- ✓ Widely used in the food industry for their gelling, thickening, and stabilizing properties
- ✓ Used in pharmaceutics as inactive excipient in pills/tablets
- ✓ GRAS substance

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

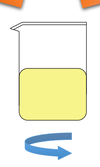


- ✓ Rapid onset of action and intermediate duration of efficacy
- ✓ Widely employed to relieve itching, burning, and pain from skin inflammations, injected as a dental anaesthetic,
- ✓ Already used as local anaesthetic in wound healing

WAFERS PREPARATION

Carrageenan

Hyaluronic Acid
HYASIS® (Novozymes)

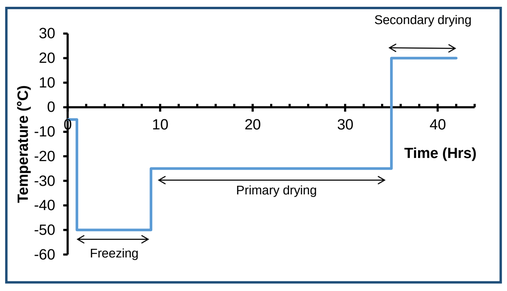


Mixing 40°C

Freeze drying

CARR/HA composite wafers

Freeze drying cycle



Wafer composition

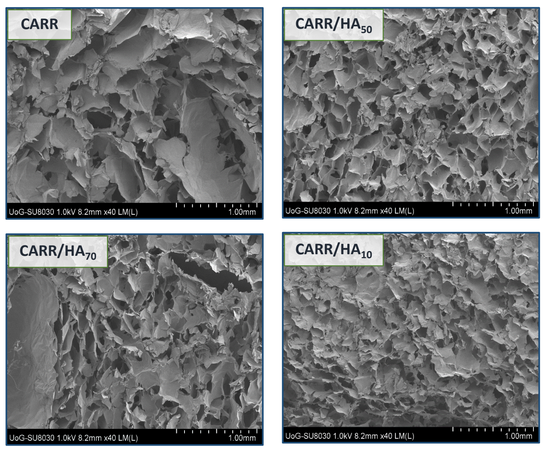
Sample*	CARR (% w/w)	HA (% w/w)	LID Loading (%)
CARR	100	-	10
CARR/HA_{50}	50	50	10
CARR/HA_{30}	70	30	10
CARR/HA_{10}	90	10	10

*All gel formulations are at 2% w/v

- 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

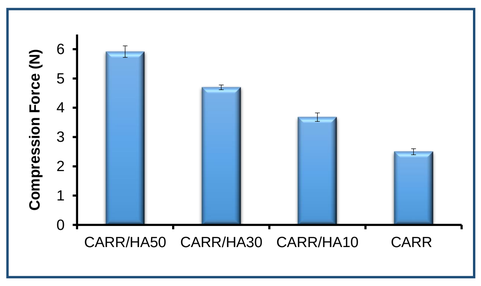
Scanning electron microscopy



Some properties of the wafers

	Porosity (%)	Density (mg/cm³)	Water absorption (%)	Water Retention (%)	EWC (%)
CARR	82.25 ± 4.53	36.78 ± 1.51	3782.7 ± 86.9	67.3 ± 1.8	97,40 ± 0.09
CARR/HA_{50}	85,00 ± 2.62	30.32 ± 1.25	3640.2 ± 39,1	78.8 ± 4.1	97.33 ± 0.03
CARR/HA_{30}	87.95 ± 3.55	29.69 ± 1.75	3394.1 ± 112.5	77.1 ± 2.4	97.04 ± 0.21
CARR/HA_{10}	89.06 ± 2.98	30.55 ± 0.60	3270,7 ± 70.8	76.3 ± 1.1	97.03 ± 0.08

Wafers hardness



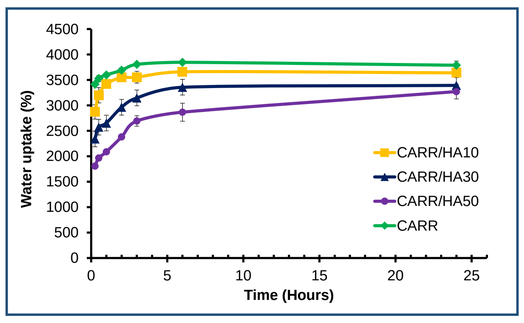
- Increase in resistance to compressive deformation with increasing concentration of HA
- More rigid wafers in presence of HA

Water uptake

Wafers of known weight were placed into beakers of test solution. The dressings were removed from the solution at periodic intervals (0.5-48 hours) and gently blotted to remove excess liquid from the outer surface. The hydrogels were then reweighed. The water uptake of hydrogels was calculated by the following equation:

$$(\%) = (W - W_0)/W_0 * 100,$$

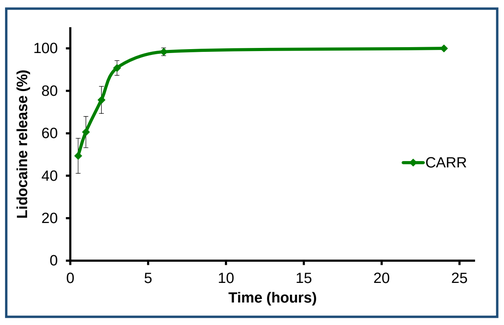
where W_0 and W represent the weight of the hydrogels before and after the experiment



The presence of HA within the wafers decreases water uptake

Preliminary Lidocaine release

Wafers of known weight were placed on a wire mesh into a custom made release chamber using Simulated Wound Fluid (SWF) as dissolution media. The dissolution medium was constantly stirred throughout the experiment using a magnetic bar and the temperature was maintained at 37°C. 1 ml aliquot of dissolution media were withdrawn at predetermined time intervals and analyzed by HPLC. The same amount of new media was added to maintain constant the volume during the experiment.



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

Resistance to compression

Depth of compression (mm)	CARR: Mean peak force (N) (±s.d.)	CARR: Relaxation distance (mm) (±s.d.)	CARR: Compression recovery ratio (±s.d.)	CARR: Compaction (mm) (±s.d.)
0.2	0.38 (0.06)	0.16 (0.01)	0.81 (0.02)	0.02 (0.04)
0.5	0.62 (0.08)	0.45 (0.03)	1.13 (0.08)	0.05 (0.03)
1	1.58 (0.06)	0.81 (0.03)	1.24 (0.05)	0.19 (0.03)
2	2.50 (0.10)	1.37 (0.04)	1.47 (0.04)	0.63 (0.04)
3	6.65 (0.21)	1.83 (0.02)	1.64 (0.02)	1.17 (0.02)

Depth of compression (mm)	CARR/HA_{50}: Mean peak force (N) (±s.d.)	CARR/HA_{50}: Relaxation distance (mm) (±s.d.)	CARR/HA_{50}: Compression recovery ratio (±s.d.)	CARR/HA_{50}: Compaction (mm) (±s.d.)
0.2	1.04 (0.57)	0.18 (0.01)	1.13 (0.02)	0.02 (0.00)
0.5	2.27 (0.07)	0.35 (0.01)	1.43 (0.04)	0.15 (0.01)
1	4.22 (0.43)	0.62 (0.01)	1.63 (0.04)	0.38 (0.01)
2	5,92 (0.20)	1.04 (0.12)	1.95 (0.26)	0.96 (0.12)
3	8.61 (0.76)	1.49 (0.09)	2.03 (0.10)	1.51 (0.09)

Depth of compression (mm)	CARR/HA_{30}: Mean peak force (N) (±s.d.)	CARR/HA_{30}: Relaxation distance (mm) (±s.d.)	CARR/HA_{30}: Compression recovery ratio (±s.d.)	CARR/HA_{30}: Compaction (mm) (±s.d.)
0.2	0.61 (0.10)	0.18 (0.01)	1.16 (0.03)	0.02 (0.00)
0.5	1.57 (0.18)	0.37 (0.04)	1.40 (0.21)	0.13 (0.04)
1	3.49 (0.54)	0.54 (0.68)	1.47 (0.04)	0.32 (0.02)
2	4.47 (0.08)	1.12 (0.02)	1.74 (0.04)	0.88 (0.02)
3	5.54 (0.87)	2.12 (0.12)	1.43 (0.08)	0.88 (0.12)

Depth of compression (mm)	CARR/HA_{10}: Mean peak force (N) (±s.d.)	CARR/HA_{10}: Relaxation distance (mm) (±s.d.)	CARR/HA_{10}: Compression recovery ratio (±s.d.)	CARR/HA_{10}: Compaction (mm) (±s.d.)
0.2	0.43 (0.06)	0.20 (0.01)	1.01 (0.02)	0.02 (0.04)
0.5	1.04 (0.11)	0.37 (0.05)	1.39 (0.20)	0.13 (0.05)
1	2.16 (0.09)	0.71 (0.01)	1.42 (0.03)	0.29 (0.01)
2	3.68 (0.15)	1.25 (0.04)	1.61 (0.06)	0.75 (0.04)
3	4.81 (0.37)	1.68 (0.23)	1.87 (0.16)	1.32 (0.23)

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

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

📖 Catanzano O. *et al.* Carbohydrate Polymers (2015), in press; Kianfar F. *et al.* Colloids Surf B Biointerfaces. 2013 Mar 1;103:99-106; Boateng J.S. *et al.* Int J Pharm. 2010 Apr 15;389(1-2):24-31; Pawar H.V. *et al.* J Pharm Sci. 2014 Jun;103(6):1720-33.