Fiber-Hydrogel Sandwich-Like Composites with Improved Antimicrobial Protection

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Introduction

Chronic wounds (CW) are described as a global health problem. Typically, these wounds are characterized by defective cell matrices, high microbial concentration, dysregulated moisture, and uncoordinated, self-sustained inflammation. Considering conventional dressings present a passive action against microorganisms, new interactive and bioactive structures based on hydrogels and nanofibers (resemblance with extracellular matrix) have been explored.

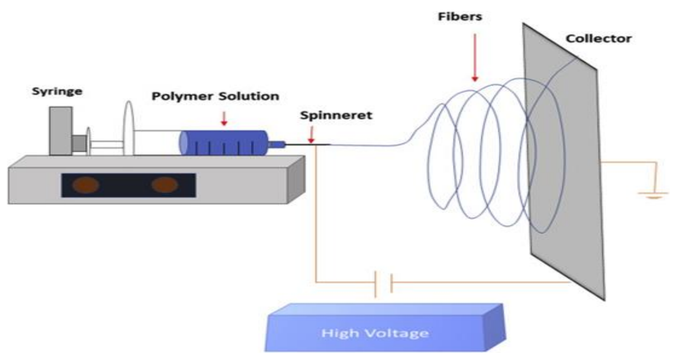
Goal of this Research

Production of a multifunctional sandwich-like system for fight CW infections, to overcome the limitation of the conventional wound dressings. Made of three layers: (outer) nanofibrous mat of polycaprolactone (PCL) (middle) sodium alginate (SA); and (inner) a second nanofibrous mat composed of PCL and polyethylene glycol (PEG) for facilitated cell integration and recognition, reduced hydrophobicity and complementary antimicrobial effects

Materials and Methods

Electrospinning

Spinning technique that allows the production of continuous, homogeneous nanofibers films.



Polymeric solution preparation

PCL 14% and PCL/PEG in in chloroform/dimethyl formamide (CHF/DMF at 9/1 v/v). SA 2% in dH2O.

Electrospinning processing conditions

Potential: 12 kV
Extruding Speed: 0.7 mL/h
Distance to Collector: 17 cm
Needle (inner diameter): 18 gauge.

Active agents Minimum Inhibitory Concentrations (MICs)

The antimicrobial potential of the Ampicillin and do polymer PEG were examined for their minimum inhibitory concentrations (MICs) against Gram-positive bacteria, *Staphylococcus aureus (S. aureus*) and Gram-negative bacteria, *Escherichia coli (E. coli)*.

Antibacterial Evaluations	*S. aureus* (ATCC 6538)		*E. coli* (ATCC 25922)	
	MIC (mg/mL)	MBC (mg/mL)	MIC (mg/mL)	MBC (mg/mL)
Ampicillin	0.004	0.004	0.128	0.064
PEG (Mw 300)	64.0	128.0	256.0	256.0

Active agents loading

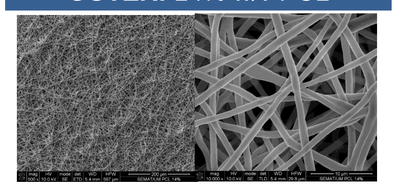
Polymer loading for the fibers production: PEG polymer is added to de PCL (14%) solution at MBC concentration (256 mg/mL).

Antibiotic loading for hidrogel production: After the hydrogel solution (SA 2% dilution in dH_2O), the solution of Ampicillin at 100 × MBC (6,4 mg/mL) diluted in dH_2O was added and lived in agitation (150 rpm) for 1 h.

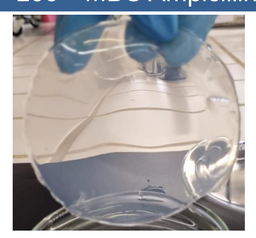
Result and discussion

Dressing morphology

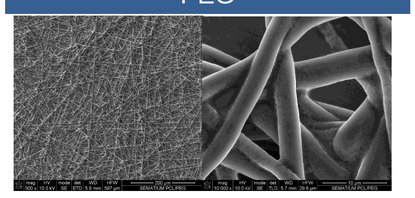
OUTER: 14% w/v PCL



MIDDLE: 2% w/v SA + 100 × MBC Ampicillin

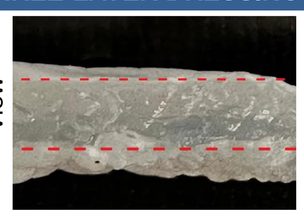


INNER: 14% w/v PCL + 1 × MBC PEG



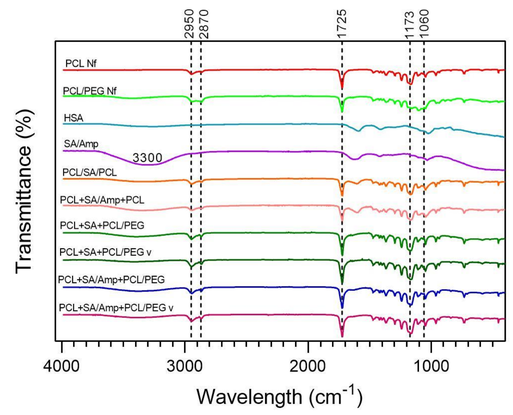
Complete Formulation: THREE-LAYER DRESSING

Cross-Section View



Top View

Components identification and Thermal Beaver

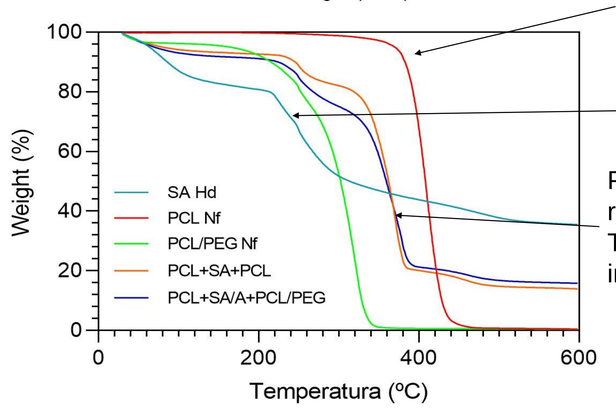


PEG only caused a reduction of the peak at 1173 cm^{-1} (C-O-C interactions)

Ampicillin (A) was not detected

Characteristic peaks of PCL (1725 cm^{-1} of C=O group) and SA (1600 cm^{-1} of COO^- group) were identified.

Additives (A and PEG) did not alter the spectra. Their presence was masked by the main polymers PCL and SA.



Additives reduced thermal stability of PCL (first degradation step at approximately 360ºC)

SA hydrogel experience faster thermal degradation, particularly after 220ºC

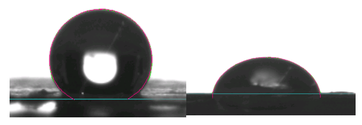
Presence of PCL nanofibers improved the thermal response of the hydrogel-based system. The additives ampicillin (A) and PEG had little impact on the thermal response of the dressing.

*Hd = hydrogel; Nf = nanofibers; A = ampicillin

Wettability and Hydration Capacity

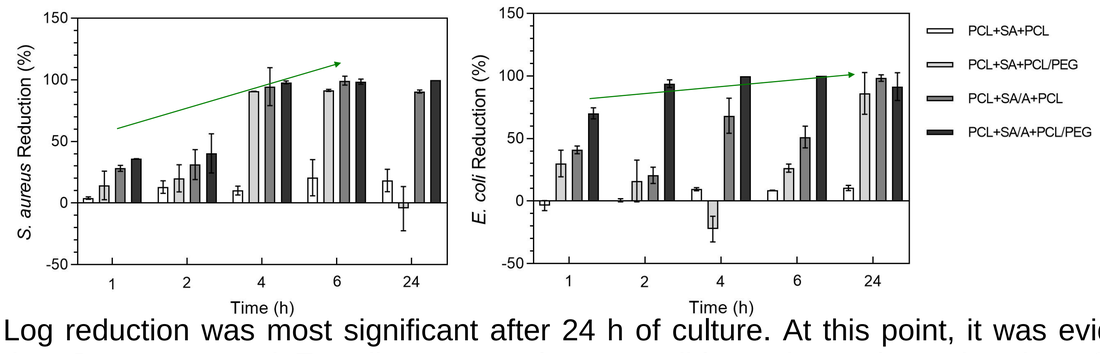
Contact Angles of Nanofiber Mats:

- PCL = 124.56 ± 7.64º, **hydrophobic**
- PCL/PEG = 28.76 ± 5.01º, **hydrophilic**



Samples	Degree of Swelling (%)			
	4 h	6 h	8 h	24 h
PCL Nf	43.75 ± 0.62	-5.88 ± 0.24	16.28 ± 0.24	2.70 ± 0.25
PCL/PEG Nf	81.08 ± 0.62	70.83 ± 0.41	80.00 ± 0.50	78.79 ± 0.51
SA Hd	98.64 ± 24.19	97.38 ± 12.58	96.75 ± 9.88	95.44 ± 6.68
SA/A Hd	98.71 ± 24.65	98.29 ± 21.04	97.38 ± 12.69	94.91 ± 5.96
PCL+SA+PCL	47.78 ± 6.37	40.49 ± 5.49	41.20 ± 5.26	33.48 ± 3.81
PCL+SA+PCL/PEG	62.67 ± 2.79	49.70 ± 2.18	46.15 ± 1.89	6.67 ± 1.79
PCL+SA/A+PCL	69.98 ± 6.33	68.62 ± 6.01	67.29 ± 5.69	65.34 ± 5.66
PCL+SA/A+PCL/PEG	73.21 ± 1.43	68.09 ± 1.12	68.09 ± 1.07	74.36 ± 1.45

Antimicrobial examinations



Log reduction was most significant after 24 h of culture. At this point, it was evident that *S. aureus* and *E. coli* were equaly susceptible to the prolonged action of the Ampicillin.

Conclusion

The results demonstrated the potential of the system sandwich-like loaded with Ampicillin for applications in choric wounds for the treatment of infections.

Acknowledgments: Project UIDP/00264/2020