INCORPORATION OF *PLANTAGO MAJOR L.* EXTRACT IN POLYCAPROLACTONE ELECTROSPUN NANOFIBERS WITH POTENTIAL APPLICATION IN WOUND DRESSING

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SUMMARY

The production of biomaterials able to mimic the natural structures of the skin has been a challenge for tissue engineering. Electrospinning is a promising technique to create nanostructured films with adequate mechanical properties, making them efficient materials for the recovery of structurally damaged tissues due to the similarity with the extracellular matrix (ECM) of the skin.[1] These structural features has called attention to their application in regenerative medicine, which uses natural and synthetic polymers with the ability to encapsulate various active materials, drugs, and/or growth factors.[2] One of the most common polymers used in electrospinning is polycaprolactone (PCL) which is a biodegradable polyester, highly used in the production of medical devices due to its good biocompatibility.[3] Plantago Major L (*P. major*) is a perennial plant with origin in Europe.[4] The *P. major* have been used traditionally in regenerative medicine due to their excellent anti-inflammatory, analgesic, anti-ulcer, antibiotic, etc. characteristics, which makes it a promising phytopharmaceutical drug for biomedical and regenerative application.[5] The main goal of this work was to develop a PCL loaded with hydroalcoholic extract of *P. major* for its application in wound healing. Initially,

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the hydroalcoholic extract from leaves was produced [1:1].[6] A study of the minimum inhibitory concentration of the extract using two strains of *Staphylococcus aureus*, one resistant (MRSA) and other sensitive to methicillin (MSSA), was carried out. It was possible to maintain inhibition of the growth for both strains until a dilution of the extract in 25% (v/v). Four solutions were prepared with and without the extract, using two different solvent systems, following previous studies performed in our research group.[7] The first solvent system was prepared using acetic acid (AA) and formic acid (FA) with a volumetric ratio AA:FA= 9:1, while the second solvent system was developed with dichloromethane (DCM) and dimethylformamide (DMF) and volume ratio DCM:DMF=7:3. The solution was mixed at 30 °C for 3 hours. A 25% (v/v) solution of the *P. major* extract was added for each solvent system and magnetically stirred for another half hour. Subsequently, the four solutions (with and without extract) were taken for electrospinning varying the flow rate, voltage, and tip needle-collector distance. The fibers produced with AA/FA presented smaller diameters with and without extract (152.3 ± 67.9 nm) compared with DCM/DMF solutions (335.5 ± 146.1 nm). The extract incorporation did not affect the morphology and the diameter of fibers. Finally, an antimicrobial test of the films (from DCM/DMF solvent-system) in both *E. coli* and *S. aureus* (MSSA*)* was carried out, showing that the used extract presented better bactericide action in gram-negative bacteria (*E. Coli*) while Gram-positive bacteria (*S. aureus*) do not present significant variation compared with the control group. In conclusion, PCL nanofibers with incorporated *P. major* extract were successfully prepared. The smallest fibers diameters were obtained for the AA/FA polymer solutions. However, this solvent system can lead to possible degradation of the extract, attributed to the acid character of the solvent. The antimicrobial capacity of the extract from *P. major* leaves for gram-negative bacteria was confirmed.

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