Local delivery of doxorubicin nanocrystals from electrospun nanofibers

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Doxorubicin (DOX) is a class I (high permeability and high solubility) anthracycline antibiotic widely used as a chemotherapeutic drug for treating many types of cancers. It can annihilate cancerous cells by damaging DNA and its replication via the mechanisms of intercalation between nucleotides, by inhibition of topoisomerase II and by generating oxygen free radicals [1]. However, free DOX is known to have a very low therapeutic index and repeated administration of high doses are required to achieve the desirable therapeutic effect, which causes severe side effects to normal tissues like cardiotoxicity and myelosuppression [2]. So, the development of suitable carrier systems for local treatment of cancer recurrence is necessary. Recent studies indicate that an enhanced therapeutic efficacy can be achieved by using nanocarriers that accomplish rapid drug release once they arrive at the tumor site [2]. It is recognized that the use of electrospun nanofibers for drug carriers is very promising in the biomedical field, mainly for the local chemotherapy postoperation [3].
The objective of this study is to develop a novel system for local application of DOX either in surgical locci or in a topical application device ennabling a controlled release of the drug. The developed system involves the encapsulation of DOX into electrospun polymeric nanofibers. Chosen polymers are polyoxyethilene (PEO) and polycaprolactone (PCL). Fig. 1 shows as an example of a PCL fiber mat containing DOX.

Fig. 1 DOX-PCL nanofibers mat produced by electrospinning

Nanofibers' composition and preparation method were optimized for the two polymeric systems. Topographic and elemental analysis were done by Scanning Electron Microscopy with Energy-Dispersive X-ray Spectroscopy (SEM-EDS) evidencing the presence of DOX inside the fibers. Structural characterization of the produced nanofibers were achieved by X-ray diffraction also showing the DOX nanocrystals inside the fibers. In order to elucidate the interactions between the polymer and the DOX, Attenuated Total Reflectance Fourier Transform Infrared Spectroscopy (ATR-FTIR) was used. Controlled release assays were carried out at cancer tissues' conditions (pH 5.5 and 37 ºC) using a dialysis tubing with a cut-off of 3.5 kDa. The kinetics of DOX release from PEO-loaded and from PCL-loaded nanofibers was established and can be tailored adjusting electrospinning conditions and drug load capacity. The sulforhodamine B (SRB) assay was also performed to measure drug-induced cytotoxicity and cell proliferation in human colon cancer cell lines RKO and SW480.

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Acknowledgments: We thank PARALAB for the SEM-EDS analysis and Dr. A. S. Azevedo for the X-ray analysis. This work was supported by the Portuguese Foundation for Science and Technology (FCT) in the framework of the Strategic Funding UID/FIS/04650/2013. Marlene Lúcio acknowledges the exploratory project funded by FCT with the reference IF/00498/2012.