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DEVELOPMENT OF BIODEGRADABLE NANOCAPSULES CONTAINING ANTICOAGULANT FOR USE IN VASCULAR TISSUE ENGINEERING

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Synthetic vascular grafts are widely used in surgical procedures for revascularization of medium and large vessels. However, when applied in vessels with < 6 mm diameter, the synthetic grafts have a high failure rate, mainly due to the formation of thrombi in their lumen. Thus, new vascular grafts should be developed for application in small diameter vessels, with the ability to prevent thrombus formation. An alternative method to prevent thrombosis is to associate the vascular grafts with anticoagulants. These drugs can be encapsulated into nanoparticles that allow their controlled and local release. Thus, the aim of this work has been to develop biodegradable nanocapsules containing heparin for further association into vascular grafts. Nanocapsules (NCs) were developed using poly(lactic-co-glycolic acid) (PLGA) by the electrospraying technique (ES). For the production of NCs, an aqueous phase was prepared with 0 (control) or 1,000 UI of heparin (Hep). This aqueous phase was added to an organic phase, consisting of 0.2 g PLGA, 5 mL chloroform, 0.6 mL triglyceride mixture and 0.06 g Span 80. After homogenization, the resulting emulsions were subjected to ES process. Different ES parameters were tested until homogenous and round capsules were observed under optical microscope. The diameter, polydispersity index (PdI) and zeta potential were evaluated by ZetaSizer (Malvern Nano-S). The morphology of NCs was analyzed by scanning electron microscopy (SEM). For analysis of heparin content, 10 mg of nanocapsules were collected, diluted in 2 mL of H2O and vortexed. The supernadant was analyzed by toluidine blue test. When the control emulsion (0 mg Hep) was submitted to ES, spherical capsules were obtained with 15 kV of tension, 15 cm of distance between needle and collector plate and 0.6 mL/h of flow rate. When 1,000 UI of Hep was added, the voltage needed to be adjusted to 14 kV. The control NCs showed 178.8 ± 3.7 nm of average diameter, 0.326 ± 0.04 of PdI and -23.4 ± 1.5 mV of zeta potential. The Hep NCs showed 262.6 ± 14.6 nm of diameter, 0.291 ± 0.01 of PdI and -28± 2.5 mV of zeta potential. The determined amount of heparin in nanocapsules was 4.4 ?g/mL. Biodegradable NCs were successfully produced by the ES technique and the addition of heparin did not alter its morphology and stability. The heparin NCs can be easily associated with biomaterials for use in vascular grafts in tissue engineering and regenerative medicine.