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Novel polymer for gene and stem cell delivery

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The disulfide-linked bioreducible polymer poly (cystaminebisacrylamide-diaminohexane) [CBA-DAH] was synthesized. Primary rat skeletal myoblasts were transfected with poly (CBA-DAH)/pCMV-VEGF165. MRI analysis of the treatment groups revealed a significant recovery of ejection fraction in the VEGF myoblast treatment over myoblasts only and ligation control. Apoptotic cell population revealed a significant attenuation of apoptosis in the myoblast only group but a higher attenuation in the VEGF myoblast group compared to ligation controls. This indicated that while myoblast implantation alone limits apoptosis in the myocardium, the VEGF myoblast group is producing a significantly higher protective effect. The work demonstrates that bioreducible polymers can successfully be used to transfect skeletal myoblasts with angiogenic factors. We proposed that the hMSCs delivered by our PLGA/PEI 1.8k (PPP) microparticles produce in vivo cardioprotective effects on post-infarct cardiac remodeling. We demonstrated that intramyocardial delivery of hMSCs by porous PPP particles in infarcted rats preserved engraftment of hMSCs in infarcted myocardium, cardiac geometry, and left ventricular systolic function. In addition, hMSCs-loaded PPP delivery augmented blood flow to coronary artery. The reduced infarct size of hMSC-loaded PPP delivery was followed by a decrease in fibrosis, protection from cardiomyocyte loss, and down-regulation of apoptotic activity. Furthermore, the increased angiogenesis and decreased myofibroblast density in the border zone of the infarct support the beneficial effects of hMSC-loaded PPP administration. These results of hMSC therapy delivered by PPP particles provide insight into the hMSC therapy translation in the treatment of acute myocardial infarct to human trials.

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Liposomal voriconazole (VOR) formulation for improved ocular delivery

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Treating infectious eye diseases topically requires a drug delivery system capable of overcoming the eye's defense mechanisms, which efficiently reduce the drug residence time right after its administration, therefore reducing absorption. In order to try to surpass such administration issues and improve life quality for patients with fungal keratitis, liposomal voriconazol (VOR) formulations were prepared. Formulations were composed of soy phosphatidylcholine (PC) containing or not 1, 2-dioleoyl-3-trimethylammonium-propane (DOTAP) and cholesterol. Liposomes were characterized by their drug entrapment efficiency (EE), drug recovery (DR), average diameter (size) and polydispersivity index (PdI). In vitro mucosal interaction and irritancy levels, *ex* vivo permeation, as well as the short-term stability were also assessed. Liposomal VOR formulation produced with 7.2:40 mM VOR:PC showed to be the most promising formulation: Mean size of 116.6±5.9 nm, narrow PdI (0.17±0.06), negative zeta potential (~ -7 mV) and over 80% of EE and yield, remaining stable for at least 30 days in solution and 90 days after lyophilization. This formulation was classified as 'non-irritant' after HET-CAM's test and was able to deliver about 47.85±5.72 µg/cm2 of VOR into porcine cornea after 30 min of permeation test. Such drug levels are higher than the minimal inhibitory concentrations (MIC) of several fungi species isolated from clinical cases of corneal keratitis. Overall results suggest VOR can be effectively incorporated in liposomes for potential topical treatment of fungal keratitis. This work was supported by CNPq, CAPES, FAPDF and L'Oreal-UNESCO for the Women in Science Awards.

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