MODIFIED NANOPRECIPITATION METHOD FOR THE PREPARATION OF GENTAMICIN-LOADED PLGA-PEG NANOPARTICLES

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Purpose:
The aim of this study is to perform a detailed investigation of the experimental parameters involved in gentamicin loading process into nanoparticles using PLGA and PLGA-PEG, as the biodegradable polymers. The nanoparticle formulations (Np) should guarantee the antibiotic sustained release, and its delivery into the intracellular infection minimizing adverse effects and nefro-and oto–toxicity. The high aqueous gentamicin solubility represents the main criticality in achieving Nps with high drug payload.

Methods:
The nanoprecipitation technique was selected and modified for the encapsulation of Gentamicin (Gent). Eight batches were prepared as 2^3 screening design to study the effect of polymer concentration (25-12.5 mg/ml), stirring rate (700-350 rpm) and solvent (S)/non-solvent (nS) ratios (0.2-0.5 v/v) on particle size, size distribution (PI) and drug loading (DL). Further experimental parameters were investigated to optimize the drug loading: solvent (S) and non-solvent (nS) nature, polymer composition (PLGA-uncapped and PLGA-PEG), addition of tonicity agent and PVA solution, pH. The resulting Np were characterized for their morphology, particle size and PI, zeta potential and DL. Nanoparticles lyophilization process was investigated by the following cryprotectants: sucrose, trehalose, mannitol and related mixtures.

Results:
The following optimized experimental conditions for Np preparation were deduced from the 2^3 screening design: 12.5 mg/ ml polymer concentration, 700 rpm stirring rate and 0.5 ratio S/nS, and they were confirmed by the good results in terms of nanoparticles size (240 nm), PI (0.1) and ζ (-0.86 mV). The temperature and time used for solvent evaporation were suitably set up at 4°C and 5hr in order to achieve Nps easy resuspension after centrifugation. The addition of ethanol in the PVA solution permitted to increase the drug loading from 5 to 12.53 µg/ mg NPs. The drug loading was further improved when mixtures of PLGA-uncapped and PLGA-PEG were used (> 20 µg/mg Nps). The best results, in terms of nanoparticles resuspendability and particle size distribution preservation after freezedrying, were observed with the addition of 100% w/w of sucrose.

Conclusion:
Gent is effectively entrapped in PLGA-PEG/PLGA Nps by the modified nanoprecipitation method. The enhanced drug loading can be obtained by varying the experimental conditions.