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Insights into non-viral vectors for gene therapeutics

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Gene delivery has shown a great promise in pre-clinical and clinical trials, with new treatment options for a number of diseases. Non-viral gene therapy with cyclodextrins as vectors for gene delivery has gained more interest due to overcoming problems of viral vectors such as immunogenicity, mutagenicity and oncogenicity. Cyclodextrins interaction with enclosed DNA results in condensation of DNA which should remain stable and protected from nuclease digestion and hence be efficiently delivered into cells. The purposes of this research were to stabilize the deoxyribonucleic acid (DNA) via using β- and γ-cyclodextrins (CD) to condense and include the DNA; to evaluate the influence of co-polymers (poly 1-vinylpyrrolidone-co-vinylacetate and Pluronic F127) and their concentrations on stability of DNA-CD complexes, encapsulation efficiency of DNA and charge of the DNA formulations and to study the effect of drying of formulations on DNA stability. The DNA (from calf thymus), CDs and copolymers were dissolved in phosphate buffer saline (pH 7.4) in different concentrations. Freshly prepared and dried DNA formulations were evaluated after storage at ambient temperature (25˚C). UV-Vis spectroscopy and fluorescence were used to study DNA stability and inclusion efficiency, respectively. DNase I activity measurement was used to assess availability of the DNA outside the CD complexes; Fourier Transform Infra-Red (FT-IR) investigates interactions of excipients in inclusion complexes with the DNA and the charge was measured employing zeta potential. Scanning Electron Microscopy (SEM) was applied to study the morphology of dried DNA samples. The γ-CD significantly ($p<0.05$) enhanced DNA protection against DNase I degradation and β-CD led to higher ($p<0.05$) DNA inclusion. The interactions between excipients and the DNA stabilize the DNA; this has been confirmed by FT-IR results and by the DNase I test (for example: there was only 0.92µg DNA/mL loss from fresh solution of 200 µg β-CD/mL with 20µg DNA/mL and 100µg poly 1-vinylpyrrolidone-co-vinylacetate/mL formulation kept at ambient temperature for two weeks; the DNA inclusion in the same formulation, as determined by the fluorescence spectroscopy, was 28.8%). For dried samples in the presence of β-CD, particles show uniform size and shape as indicated by the SEM. Excipients concentration had no effect on percentage inclusion of DNA within CDs. The presence of poly 1-vinylpyrrolidone-co-vinylacetate with either β-CD or γ-CD resulted in formation of positively charged DNA-CD complexes and this is desirable for cell transfection. In conclusion, cyclodextrin complexes in the presence of copolymers protect DNA. The copolymers/CDs led to formation of positively charged DNA complexes which is favorable for cell transfection.

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Develpoment and characterization of clarithromycin loaded porous scaffold film as wound dressing material

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In the present study, porous scaffold films of Clarithromycin were prepared by the process of solvent casting method. The porous films were prepared using chitosin dissolved in acetic acid in different concentrations and PEG-4000 which works as plasticizer and porosity enhancer. The preliminary drug identification studies showed that drug confers to all standard values for solubility, melting point, UV and IR. Porous films prepared by solvent casting method with different polymer concentrations were subjected to various investigations namely moisture content, water absorption ratio, swelling index, porosity, folding endurance, tensile strength, entrapment efficiency and in-vitro drug release. Formulation FB4 was found to be an optimized formulation with moisture content 4.36±0.316, water absorption ratio 245±1.57, swelling index 219.47±3.66, porosity 54.71±0.737, folding endurance 213±4.16, tensile strength 43.7 mJ/cm2 and in-vitro drug release 99.64±0.88 for 12 hrs. From the present study we concluded that porous scaffold film of Clarithromycin was successfully prepared by solvent casting method using chitosin polymer in different ratio with PEG-4000 to achieve a controlled and efficient release of the drug. Overall the porous scaffold films offered potential advantage of high drug loading capacity (up to 99%) and homogenous drug dispersion.

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