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TARGETED PLGA NANOPARTICLES FOR GENE DELIVERY IN CHARCOT-MARIE-TOOTH DISEASE

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Abstract: In this study, PVA-modified PLGA nanoparticles were synthesized for the treatment of Charcot-Marie-Tooth (CMT) disease. Following the encapsulation of therapeutic plasmid DNA (pDNA), the nanoparticle surface was functionalized with a targeting peptide to guide the nanocarrier to TMPRSS5, a receptor preferentially expressed on Schwann cells [**1,2**]. Different PLGA terminal group chemistries were examined, to optimize nanoparticle formation and performance. The resulting nanocarriers were characterized using physicochemical techniques, such as DLS and SEM, to evaluate size, morphology, and encapsulation efficiency.

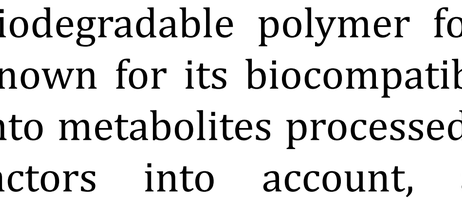
• Introduction

Nanotechnology has emerged as a powerful tool in healthcare, particularly in drug and gene delivery. Nanoparticles (NPs) overcome key limitations of conventional therapies by improving drug encapsulation and targeted delivery, making them suitable for the treatment of Charcot–Marie–Tooth (CMT) disease. PLGA (poly(lactic-co-glycolic acid)) is a widely used biodegradable polymer for the development of nanocarriers, known for its biocompatibility and low toxicity, as it degrades into metabolites processed via the Krebs cycle [**3**]. Taking these factors into account, appropriately PVA-modified PLGA nanoparticles (NPs) could meet all the requirements for the efficient transport and delivery of the genetic material to the target neurons.

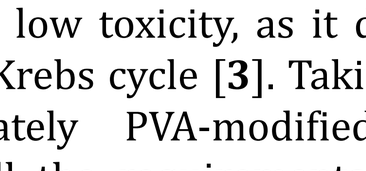
• Materials and methods

Materials: PLGA (Acid Terminated), PLGA (Ester Terminated), PVA, pDNA (264-PO-EGFP-WPRE), EDC/NHS, Gln-Ala-Arg-AFC-TFA salt.

Preparation technique: Double emulsification (**Fig. 1)**, solvent evaporation, 25 °C and 3 h.



PLGA



PVA

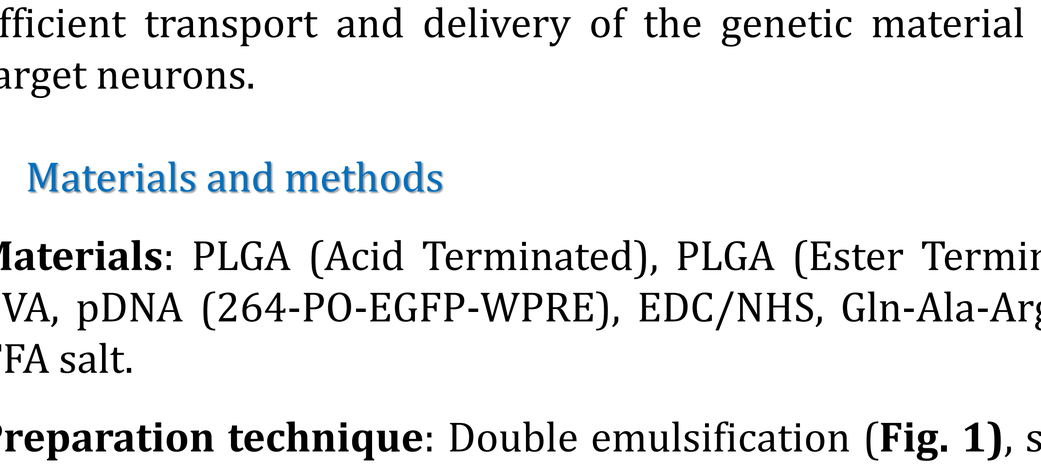


Fig. 1: Nanoparticle production method

• Results and Discussion

Peptide conjugation efficiency depended on PLGA terminal chemistry, reaching ~60% for ester-terminated and ~95% for acid-terminated PLGA. Moreover, DLS analysis revealed a particle size with no peptide and pDNA of 302±3 nm (E.T.) and 537±13 nm (A.T), with FT-IR spectra verifying the presence of both PLGA and PVA, as shown in **Fig. 2**.

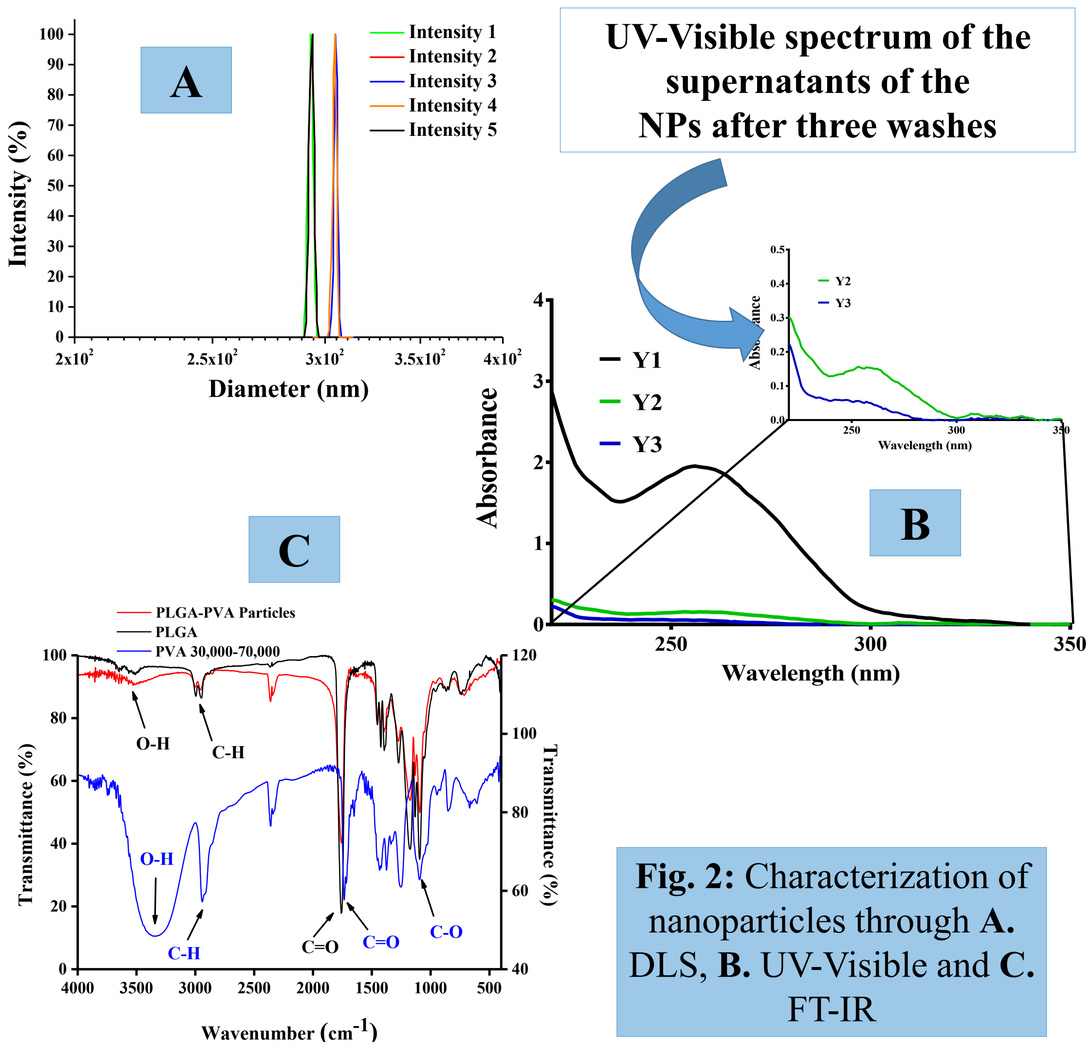


Fig. 2: Characterization of nanoparticles through **A.** DLS, **B.** UV-Visible and **C.** FT-IR

• Conclusions

Acid-terminated PLGA exhibited significantly higher peptide conjugation compared to ester terminated PLGA. A moderate pDNA encapsulation efficiency was achieved, indicating that alternative synthesis strategies should be further explored. Overall, the physicochemical properties of the PLGA NPs support their bioprofile in CMT disease therapeutics.

References:

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