Design and Characterization of Novel Imatinib-Loaded Nanoparticles for Localized Immunomodulation

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Current autoimmune disease therapies involve drugs that have a wide range of side effects due to the generalized immunosuppression that suppresses healthy cells in the process. This study discusses the design and immunomodulatory effect of poly(lactic-co-glycolic acid)-poly(ethylene glycol)-maleimide-based nanoparticles (PLGA-PEG-MAL) as a carrier for imatinib, an immunosuppressive drug. ILNPs were synthesized using nanoprecipitation and measured with dynamic light scattering to have an average hydrodynamic diameter of approximately 34 nm, which is the ideal size for phagocytosis and allows these particles to be rapidly uptaken by autoreactive cells in inflamed areas, allowing for sustained drug release within the cell and preventing excess drug from leaking into other areas of the body. Lyophilization and UV-Vis spectroscopy results demonstrate that these ILNPs have a high encapsulation efficiency of 83.2%. In vitro human macrophage assays show that ILNPs increase surface expression of VISTA and decrease expression of CD86 while maintaining expression of CD11c and HLA2, demonstrating that ILNPs promote macrophage differentiation towards the anti-inflammatory phenotype without compromising cell function or viability, and this phenotypic shift can prevent the need for chronic drug usage. These ILNPs also have the potential to be used as an allergy immunotherapy due to the presence of a maleimide tail that allows for the attachment of antigens that can ensure that only antigen-specific cells uptake these ILNPs and are suppressed. The cost of the raw materials to synthesize these ILNPs is $12.22 per batch, demonstrating the potential of ILNPs to be an effective and affordable immunotherapy for both autoimmune diseases and allergies.

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