Using Dendrimers and PLGA Nanoparticles for Targeted Drug Delivery to Treat Neuroinflammation

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Neuroinflammation occurs when microglia become activated and release neurotoxic factors. This process plays a key role in a number of neurological disorders, including Alzheimer's disease, Parkinson's disease, and multiple sclerosis. Treatments for neuroinflammation are currently limited. N-acetylcysteine (NAC) is an inexpensive therapeutic candidate, but the drug is limited by its hydrophobicity and poor bioavailability. The objective of this study was to develop nanocarriers that can efficiently transport NAC to microglia and thus enhance its anti-inflammatory activity. Poly(amidoamine) (PAMAM) dendrimers and biodegradable poly(lactic-co-glycolic acid) (PLGA) nanoparticles (NPs) were investigated, as both have emerged as promising drug delivery vectors. The conjugation of PAMAM and NAC was optimized for a high drug payload, as confirmed by nuclear magnetic resonance spectroscopy. Novel NPs were fabricated by encapsulating PAMAM-NAC in PLGA. Dynamic light scattering, scanning electron microscopy, and confocal microscopy revealed the NPs' propensity for drug delivery by receptor-mediated endocytosis. The drug systems, containing equivalent NAC concentrations, were evaluated in murine microglial cells activated by lipopolysaccharide. Accumulation of nitric oxide (NO) was measured as an indicator of inflammation. NAC alone produced no significant reduction in NO levels, whereas PAMAM-NAC and conjugate-loaded PLGA NPs were able to reduce NO production by up to 64% and 85%, respectively. The treatments did not impact cell viability, suggesting that they could potentially be used in clinical applications. Shown by their improved in vitro effects, the targeted drug delivery systems designed in this study may offer valuable therapies for neuroinflammation.

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