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Sialic Acid (SA)-Modified Selenium Nanoparticles Coated with a High BBB Permeability Peptide-B6 Peptide for Potential Use in Alzheimer's Disease

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Abstract

The blood–brain barrier (BBB) is a formidable gatekeeper toward exogenous substances, playing an important role in brain homeostasis and maintaining a healthy microenvironment for complex neuronal activities. However, it also greatly hinders drug permeability into the brain and limits the management of brain diseases. The development of new drugs that show improved transport across the BBB represents a promising strategy for Alzheimer's disease (AD) intervention. Whereas, previous study of receptor-mediated endogenous BBB transport systems has focused on a strategy of using transferrin to facilitate brain drug delivery system, a system that still suffers from limitations including synthesis procedure, stability and immunological response. In the present study, we synthesised sialic acid (SA)-modified selenium (Se) nanoparticles conjugated with an alternative peptide-B6 peptide (B6-SA-SeNPs, a synthetic selenoprotein analogue), which shows high permeability across the BBB and has the potential to serve as a novel nanomedicine for disease modification in AD. Laser-scanning confocal microscopy, flow cytometry analysis and inductively coupled plasma-atomic emission spectroscopy ICP-AES revealed high cellular uptake of B6-SA-SeNPs by cerebral endothelial cells (bEnd.3). The transport efficiency of B6-SA-SeNPs was evaluated in a Transwell experiment based on *in vitro* BBB model. It provided direct evidence for B6-SA-SeNPs crossing the BBB and being absorbed by PC12 cells. Moreover, inhibitory effects of B6-SA-SeNPs on amyloid- β peptide (A β)

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