Design and Evaluation of Multifunctional Nanocarriers for Selective Delivery of Coenzyme Q10 to Mitochondria

Anjali Sharma, Ghareb M. Soliman, Noura Al-Hajaj, Rishi Sharma, Dusica Maysinger, Ashok Kakkar

Abstract:

Impairments of mitochondrial functions have been associated with failure of cellular functions in different tissues, leading to various pathologies. We report here a mitochondria-targeted nanodelivery system for coenzyme Q10 (CoQ10) that can reach mitochondria and deliver CoQ10 in adequate quantities. Multifunctional nanocarriers based on ABC miktoarm polymers (A = poly(ethylene glycol (PEG), B = polycaprolactone (PCL), and C = triphenylphosphonium bromide (TPPBr)) were synthesized using a combination of click chemistry with ring-opening polymerization, self-assembled into nanosized micelles, and were employed for CoQ10 loading. Drug loading capacity (60 wt%), micelle size (25-60 nm), and stability were determined using a variety of techniques. The micelles had a small critical association concentration and were colloidally stable in solution for more than 3 months. The extraordinarily high CoQ10 loading capacity in the micelles is attributed to good compatibility between CoQ10 and PCL, as indicated by the low Flory−Huggins interaction parameter. Confocal microscopy studies of the fluorescently labeled polymer analog together with the mitochondria-specific vital dye label indicated that the carrier did indeed reach mitochondria. The high CoQ10 loading efficiency allowed testing of micelles within a broad concentration range and provided evidence for CoQ10 effectiveness in two different experimental paradigms: oxidative stress and inflammation. Combined results from chemical, analytical, and biological experiments suggest that the new miktoarm-based carrier provides a suitable means of CoQ10 delivery to mitochondria without loss of drug effectiveness. The versatility of the click chemistry used to prepare this new mitochondria-targeting nanocarrier offers a widely applicable, simple, and easily reproducible procedure to deliver drugs to mitochondria or other intracellular organelles.

Published In:

Biomacromolecules, dx.doi.org/10.1021/bm201538j , Vol. 13 , pp. 239-252