

ANOPARTICLES OF ANTIOXIDANT ENZYMES FOR SPINAL CORD INJURY TREATMENT

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Abstract

Numerous diseases ranging from neurodegenerative till some types of cancer are associated with overproduction of reactive oxygen species. Injection of antioxidants could decrease inflammation. Antioxidant enzymes, such as superoxide dismutase (SOD) and catalase, are the most effective antioxidants in nature and could be used to slow oxidative stress. Unfortunately, injection of native enzymes is not effective due to their rapid elimination and instability in blood. Kabanov A.V. developed nanoparticles called “nanozymes” based on block-ionomer complexes of negatively charged proteins with positively charged block-copolymers (in particular, polylysine-polyethyleneglycole, PLL-PEG). These cross-linked particles - nanozymes-1 - have nanoscale size and preserve specific activity. However, fast release of enzyme from complexes leads to fast elimination from the body. Usage of more active linkers such as glutaraldehyde leads to significant decrease in specific activity. We developed technique producing novel type of nanozymes-2. We add second negatively charged block-copolymer (poly(glutamic acid)-polyethyleneglycole (PGlu-PEG) and use protamine except PLL-PEG. This allows us to use glutaraldehyde with preserve of enzymatic activity. We were able to increased reaction yield from 5% to 45%. Developed particles have neutral charge, 50 nm hydrodynamic diameter while nanozymes-1 have slightly positive charge and 40 nm hydrodynamic diameter. Pharmacokinetics experiments showed remarkably increased T1/2 and AUC of double nanozymes versus both standard nanozymes and native SOD. To evaluate therapeutic efficiency of nanozymes rat spinal cord injury model was used. Recovery of rats was investigated with MRI imaging and BBB-test. Animals that were injected with nanozymes-2, had significant higher scores in BBB-test and lower volume of damage.

Keywords: ROS, injury, antioxidant, enzyme, SOD

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