Timed release of cerebrolysin using drug-loaded titanate nanospheres reduces brain pathology and improves behavioral functions in Parkinson?s disease

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Previous studies from our laboratory show that intraperitoneal injections of 1-metyl-4-phenyl-1,2,3,6-tetrahydropyridin (MPTP, 20 mg/kg) daily within 2-h intervals for 5 days in mice induce Parkinson?s disease (PD)-like symptoms on the 8th day. A significant decrease in dopamine (DA) and its metabolites 3,4- dihydroxyphenylacetic acid (DOPAC) and homovanillic acid (HVA) along with a marked decrease in the number of tyrosine hydroxylase (TH)-positive cells in the substantia nigra pars compacta (SNpc) and striatum (STr) confirms the validity of this model for studying PD. Since cerebrolysin (CBL) is a well-balanced composition of several neurotrophic factors and active peptide fragments, in the present investigation we examined the timed release of CBL using titanate nanospheres (TiNS) in treating PD in our mouse model. Our observations show that TiNS-CBL (in a dose of 3 ml/kg, i.v.) given after 2 days of MPTP administration for 5 days resulted in a marked increase in TH-positive cells in the SNpc and STr as compared to normal CBL. Also, TiNS-CBL resulted in significantly higher levels of DA, DOPAC, and HVA in SNpc and STr on the 8th day as compared to normal CBL therapy. TiNS-CBL also thwarted increased a-synuclein levels in the brain and in the cerebrospinal fluid (CSF) as well as neuronal nitric oxide synthase (nNOS) in the in PD brain as compared to untreated group. Behavioral function was also significantly improved in MPTP-treated animals that received TiNS-CBL. These observations are the first to demonstrate that

timed release of TiNS-CBL has far more superior neuroprotective effects in PD than normal CBL.

1-methyl-4-phenyl-1,2,3,6-tetrahydropyridin (MPTP)

Alpha-synuclein

Cerebrolysin

Cerebrospinal fluid (CSF)

Neuronal nitoic oxide synthase (nNOS)

Neuroprotection

Parkinson?s disease (PD)

Titanate nanospheres (TiNS)

1,2,3,6 tetrahydro 1 methyl 4 phenylpyridine

3,4 dihydroxyphenylacetic acid

alpha synuclein

cerebrolysin

dopamine

homovanillic acid

nanosphere

neuronal nitric oxide synthase

titanate nanosphere

tyrosine 3 monooxygenase

unclassified drug

amino acid

cerebrolysin

drug carrier

nanosphere

titanium

animal experiment

animal model

animal tissue

Article

blood brain barrier

cerebrospinal fluid

controlled study

corpus striatum

drug delivery system

drug formulation

high performance liquid chromatography

immunohistochemistry

in vitro study

in vivo study

male

mouse

neuroprotection

nonhuman

Parkinson disease

protein expression

scanning electron microscopy

substantia nigra pars compacta

timed drug release

animal

brain

C57BL mouse

drug effect

drug release

metabolism

motor activity

parkinsonism

pathology

physiology

Amino Acids

Animals

Brain

Drug Carriers

Drug Liberation

Male

Mice

Mice, Inbred C57BL

Motor Activity

Nanospheres

Parkinsonian Disorders

Titanium