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

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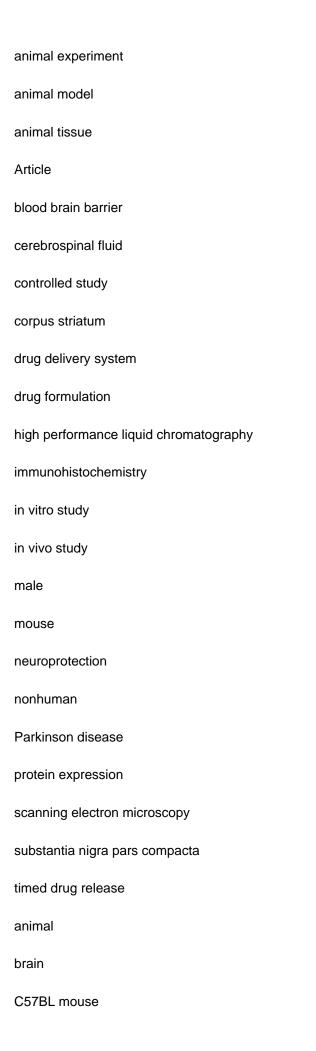
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Previous studies from our laboratory show that intraperitoneal injections of 1-metyl-4-phenyl-1,2,3,6tetrahydropyridin (MPTP, 20 mg/kg) daily within 2-h intervals for 5 days in mice induce Parkinson?s disease (PD)-like symptoms on the 8th day. A significant 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. © Springer Science+Business Media, LLC 2017. 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



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