TiO2-nanowired delivery of DL-3-n-butylphthalide (DL-NBP) attenuates blood-brain barrier disruption, brain edema formation, and neuronal damages following concussive head injury

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DL-3-n-butylphthalide (DL-NBP) is one of the constituents of Chinese celery extract that is used to treat stroke, dementia, and ischemic diseases. However, its role in traumatic brain injury is less well known. In this investigation, neuroprotective effects of DL-NBP in concussive head injury (CHI) on brain pathology were explored in a rat model. CHI was inflicted in anesthetized rats by dropping a weight of 114.6 g from a height of 20 cm through a guide tube on the exposed right parietal bone inducing an impact of 0.224 N and allowed them to survive 4 to 24 h after the primary insult. DL-NBP was administered (40 or 60 mg/kg, i.p.) 2 and 4 h after injury in 8-h survival group and 8 and 12 h after trauma in 24-h survival group. In addition, TiO2-nanowired delivery of DL-NBP (20 or 40 mg/kg, i.p.) in 8 and 24 h CHI rats was also examined. Untreated CHI showed a progressive increase in blood-brain barrier (BBB) breakdown to Evans blue albumin (EBA) and radioiodine ([131]- I), edema formation, and neuronal injuries. The magnitude and intensity of these pathological changes were most marked in the left hemisphere. Treatment with DL-NBP significantly reduced brain pathology in CHI following 8 to 12 h at 40-mg dose. However, 60-mg dose is needed to thwart brain pathology at 24 h following CHI. On the other hand, TiO2-DL-NBP was effective in reducing

brain damage up to 8 or 12 h using a 20-mg dose and only 40-mg dose was needed for neuroprotection in CHI at 24 h. These observations are the first to suggest that (i) DL-NBP is quite effective in reducing brain pathology and (ii) nanodelivery of DL-NBP has far more superior effects in CHI, not reported earlier.

Blood-brain barrier

Brain edema

Concussive head injury (CHI)

DL-3-n-butylphthalide (DL-NBP)

Neuronal injury

Neuroprotection

TiO2 nanodelivery

butylphthalide

Evans blue

iodine 131

nanowire

titanium dioxide

3-n-butylphthalide

benzofuran derivative

nanowire

neuroprotective agent

titanium

titanium dioxide

animal experiment

animal model

animal tissue

Article

blood brain barrier

brain damage

brain edema

brain tissue

concussive head injury

concussive head injury

controlled study

drug delivery system

drug efficacy

head injury

histopathology

male

nervous system injury

neuroprotection

nonhuman

parietal bone

rat

survival

animal

blood brain barrier

brain concussion

brain edema

complication

drug delivery system

drug effect

nerve cell

pathology

procedures

Wistar rat

Animals

Benzofurans

Blood-Brain Barrier

Brain Concussion

Brain Edema

Drug Delivery Systems

Male

Nanowires

Neurons

Neuroprotective Agents

Rats

Rats, Wistar

Titanium