Gedunin and its Derivatives Useful for Treatment of Neurodegenerative Diseases

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Technology description

Technical Summary

The invention comprises gedunin derivatives for the treatment of neurological disorders. These compounds are TrkB agonists, and mimic the action of the natural ligand, brainderived neurotrophic factor (BDNF). TrkB is a receptor tyrosine kinase (RTK) with high affinity for neurotrophins, polypeptide growth factors responsible for neuronal differentiation and survival via signal transduction cascades. Decreased levels of the neurotrophin BDNF has been implicated in a number of neurological disorders. Administration of exogenous neurotrophins can stimulate nerve growth and survival, but is hampered by the poor drug-like qualities of the compound including instability, poor bioavailability, and low levels of brain penetration. Synthetic peptides which mimic various domains of BDNF stimulate neuronal growth, but have not been shown to operate via a TrkB-dependent mechanism. In addition, large polypeptides with high molecular weights (ca. 2000) traditionally have proved difficult to develop with clinical success. The inventor has shown a significant reduction of infarct volume following 5 mg/kg intraperitoneal injection of deoxygedunin (38%) versus vehicle (65%) in the middle cerebral artery occlusion model in rats.

Treatment of central nervous system (CNS) disorders is an ever-increasing market. Treatment of multiple sclerosis (MS) was worth an estimated $8.1 billion in worldwide sales in 2007. Alzheimer's disease therapies were worth an estimated $5 billion, while stroke and traumatic brain injury medicines were worth an estimated $3 billion each in 2007.

Application area

Gedunin and its derivatives for the treatment of Parkinson's disease, Alzheimer's disease, HIV-related dementia, multiple sclerosis, amyotrophic lateral sclerosis, stroke, and Huntington's disease.

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