7,8-Dihydroxyflavone and its Derivatives Useful for Treatment of Neurodegenerative Diseases

Published date: March 26, 2009

Technology description

Technical Summary

The invention comprises flavone derivatives for the treatment of neurological disorders. These compounds are TrkB agonists, and mimic the action of the natural ligand, brain-derived 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 TrkB binding domains of BDNF, stimulate neuronal survivalin vitro, but have not been shown to operate in animal models. In addition, large polypeptides with high molecular weights (ca. 2000) traditionally have proved difficult to develop with clinical success. The inventor has shown various flavonoids, the most active being 7,8-dihydroxyflavone, inhibit apoptosis in a number of cellular assays via a TrkB-dependent mechanism in T48 cells and primary hippocampal neurons. Strikingly, this compound exhibits potent neuroprotective effect against neuroexcitotoxicity and stroke in mice. It also reveals robust antidepressant effect in mice.

Application area

A compound for the treatment of various neurological diseases such as Alzheimer's, Huntington's, ALS, Rett syndrome, epilepsy, Parkinson's, spinal cord injury, stroke, ischemia, brain injury, diabetic neuropathy, peripheral neuropathy, dementia, peripheral nerve injury, pain, depression and anxiety.

Advantages

Whereas current anti-depressant and anti-anxiety medications take 1-2 months to take effect, and frequently produce very harsh side effects, 7,8-dihydroxyflavone is a potent anti-depressant that demonstrates therapeutic efficacy within a few days.
A similar compound, 5,7-dihydroxyflavone, has been approved for bodybuilding use in humans.

Institution

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