Use of Razoxane for the Treatment of Alzheimer's Disease

Published date: Feb. 1, 2012

Technology description

Abnormalities in the metabolism of the transition metals, iron and copper, have been demonstrated to play a crucial role in the pathogenesis of various neurodegenerative diseases, including Alzheimer's disease (AD) and Parkinson's disease (PD). Excessive iron accumulation in the brain occurs in both AD and PD. High levels of reactive iron can increase oxidative stress-induced neuronal vulnerability, increase the toxicity of environmental or endogenous toxins, and accelerate hallmark pathologies of these diseases.

As an example among many, the expression level of amyloid-beta precursor protein (APP) that generates the AD neurotoxic peptide, amyloid-beta (A-beta), is regulated in large part by iron levels. APP mRNA has an iron response element (IRE) in its 5’ -untranslated region, and cleavage of APP to release different amyloidogenic and non-amyloidogenic peptide forms involves metalloproteases. Elevated A-beta levels as well as plaques formed by aggregation of A-beta involve iron, and play a significant role in degeneration of the brain seen in AD. Chelators can reduce both the generation and aggregation of A-beta. Razoxane, a bisdioxopiperazine, is an orally active metal chelator approved for the treatment of cancer, where it and dexrazoxane have been effectively used for decades.Market:

Up to 4.5 million Americans are estimated to suffer from AD, which usually strikes after the age of 60. Population longevity is increasing so AD is expected to be a growing health problem.

Currently marketed drugs only delay the severity of AD so better solutions are needed.

Application area

The claimed invention is the novel use of razoxane and other bisdioxopiperazines to reduce amyloid-beta peptide levels, reduce aggregation of alpha-synuclein and tau protein, and reduce abnormal protein folding or aggregation for the treatment of AD and related diseases with protein aggregation pathology. Since razoxane has been approved for humans use, it could be more quickly developed as a treatment for AD, PD and other diseases.

Advantages

In neuronal cell culture models, razoxane induced dose-dependent reductions in APP and A-beta levels without toxicity. In animal experiments (transgenic mice expressing human A-beta, razoxane substantially reduced A-beta 1-40 and 1-42 in brain by up to 46% without toxicity following once daily, 21 day administration.

Institution

NIH - National Institutes of Health

联系我们

叶先生

电 话：021-65679356

手 机：13414935137

邮 箱：yeyingsheng@zf-ym.com