Multifunctional Radical Quenchers for Mitochondrial Diseases

AzTE Cases: M10-073L, M11-096L, M12-085L, M13-038L, M15-134L, M16-269L

Invention Description

Mitochondrial diseases are a group of disorders associated with dysfunctional mitochondria, often caused by genetic mutations to mitochondrial DNA. Mitochondrial defects are damaging, particularly to tissues with high energy demands such as neural and muscle tissues. Energy effecting defects have been implicated in forms of movement disorders, cardiomyopathy, myopathy, blindness and deafness. Membrane-penetrating antioxidants are often prescribed but treatment options are limited. There have been extensive efforts to find alternative therapeutics with superior activities.

Researchers at the Biodesign Institute of Arizona State University have developed a portfolio of novel multifunctional radical quenchers (MRQs) for the treatment of mitochondrial disorders. All of the MRQs blunt oxidative stress-induced mitochondrial degradation, maintain mitochondrial membrane potential and have great intrinsic chemical stability. Cytoprotection of cultured Friedreich's ataxia cells is seen with many compounds. The alkylaminoquinone-based MRQs have a redox center which undergoes in situ redox cycling. The pyrimidinol based MRQs are able to quench lipid peroxidation as seen in FRDA lymphocytes depleted of glutathione. Some of the newer compounds have exemplary metabolic stability and bioavailability.

These compounds represent a novel class of potential therapeutics for a variety of diseases associated with decreased mitochondrial function, including Friedreich's ataxia, Leber's Hereditary Optic Neuropathy, Kearns-Sayre Syndrome, Mitochondrial Encephalomyopathy with Lactic Acidosis and Stroke-like Episodes.

Potential Applications

- Therapeutic candidates for mitochondrial diseases such as:
  - Friedreich's ataxia
  - Leber's Hereditary Optic Neuropathy
  - Kearns-Sayre Syndrome
  - MELAS (Mitochondrial Encephalomyopathy with Lactic Acidosis and Stroke-like Episodes)
  - Leigh's Syndrome
  - Amyotrophic Lateral Sclerosis
  - Diseases with significant mitochondrial component: PD, AD, Obesity, etc.

Benefits and Advantages

- Some MRQs inhibit lipid peroxidation and prevent ROS production in GSH depleted cells
- Most MRQs have greater antioxidant potential compared to α-tocopherol and idebenone
- The MRQs preserve mitochondrial membrane potential & suppress ROS
- The Coenzyme Q10 MRQs:
  - Quench reactive oxygen species (ROS) and carbon-centered lipid radicals; Augment ATP production
- The antioxidant lipophilic MRQs:
  - Have simplified synthesis routes; Suppress autoxidation of methyl linoleate; Have catalytic functionality; Augment ATP production
- The newest MRQs have great efficacy in predictive bioassays than any current agents
- Some compounds exhibit exemplary metabolic stability and bioavailability

Contact

Thomas Goodman
Vice President
Business Development, Life Sciences
Arizona Technology Enterprises, LLC (AzTE)
P: 480.884.1648
F: 480.884.1984
Tom.Goodman@azte.com
healthsciences@azte.com