

Novel Compounds for the Treatment of Cardiovascular Disease

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Technology description

Technical Summary

Electrons from NADH or FADH₂ are transported through various enzyme complexes in the mitochondria. At each step, hydrogen is transported from the matrix to the inner aspect of the mitochondria leading to a strong electrochemical gradient which ultimately is used to drive ATP synthesis by the enzyme ATP synthase. In this last step, hydrogens are also donated to oxygen to form water. It has been estimated that 1% to 3% of electrons leak from this electron transport chain and react with oxygen to form the radical superoxide. Superoxide can serve as a progenitor for other reactive oxygen species (ROS), including hydrogen peroxide, the hydroxyl radical and peroxynitrite. Importantly, various diseases lead to mitochondrial damage, increase mitochondrial leak of electrons and increase mitochondrial production of reactive oxygen species. An important aspect of this is damage to mitochondrial DNA, resulting in impaired transcription of mitochondrial proteins and further disruption of mitochondrial electron transport in a feed forward fashion.

Novel compounds have been developed as a mitochondria-targeted antioxidant. These compounds reduce mitochondrial production of ROS and prevent diseases caused by excessive mitochondrial ROS production. These include cardiovascular diseases such as hypertension, heart failure and atherosclerosis. Mitochondrial-targeted antioxidants represent a completely new class of treatments for cardiovascular disease.

Treatment of hypertension by mitochondrial-targeted antioxidant (mT) following establishment of blood pressure elevation. Following infusion of angiotensin II, mice were treated with mT or received no compound. Systolic blood pressure was measured.

Application area

Novel compositions and methods for treating cardiovascular disease.

Institution

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