



Tetrahydrobiopterin Improves Cardiac Diastolic Relaxation: A New Therapy for Diastolic Dysfunction (VA Reference No. 06-032)

Novel therapy using tetrahydrobiopterin for treatment of diastolic dysfunction associated with diastolic heart failure

Technology

Use of tetrahydrobiopterin for treatment of diastolic dysfunction

Inventor

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Key Features

- Could potentially improve diastolic function
- Administered as a dietary supplement
- Proven safe in humans for other therapies

Stage of Development

Reduced to practice with successful demonstration in vitro studies and animal models

Keywords

Therapeutic

- Cardiology
- Diastolic dysfunction
- Heart failure

Patent Status

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Technology

The Department of Veterans Affairs has developed a novel method of improving diastolic function in an endothelial nitric oxide synthase-dependent fashion with dietary supplementation of tetrahydrobiopterin (BH₄), a naturally occurring nutrient and essential cofactor of the three aromatic amino hydroxylase enzymes used in the biosynthesis of the neurotransmitters serotonin, melatonin, dopamine, norepinephrine, epinephrine, and nitric oxide.

Description

A large number of heart failure patients exhibit a relatively normal ejection fraction concomitant with diastolic dysfunction, which is the impairment of the ventricles to relax normally. This diminution of ventricular relaxation in diastolic heart failure patients leads to increased ventricular pressure making it harder for all of the blood to go into the ventricle with each heartbeat. The VA has identified that a reduction in the vascular availability of nitric oxide along with an increased production of reactive oxygen species is responsible for the initiation and/or progression of diastolic dysfunction. The endocardial nitric oxide levels are dependent on the expression of endothelial nitric oxide synthase, and BH₄ is an endothelial nitric oxide synthase cofactor, which, along with nitric oxide, is subject to oxidative depletion or destruction by excess reactive oxygen species production.

Competitive Advantage

Currently, there is no efficacious treatment for slowing the progression of or reversing diastolic dysfunction associated with diastolic heart failure. However, in leading to a new therapy for diastolic dysfunction, this invention:

- Has been shown to improve diastolic function in an animal model and could potentially improve diastolic function in humans.
- Could be administered as a dietary supplement.
- Has been proven safe and efficacious in humans, with BH₄ currently used to treat phenylketonuria.

Status

The Department of Veterans Affairs is looking for a partner for further development and commercialization of this technology through a license, and the VA inventors are available to collaborate with interested companies through a Cooperative Research and Development Agreement (CRADA).