



Technology

Use of corrin-related molecules for treatment of a variety of conditions including inflammation and low blood pressure

Inventor

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Key Features

- Corrin-related molecules have potential to scavenge NOS and inhibit NOS enzyme activity
- Could potentially be used for targeted delivery of active NOS inhibitors
- Multiple methods of administration feasible
- Demonstrated as safe and effective in humans for other conditions at both low and high doses

Stage of Development

Reduced to practice with successful demonstration in vitro studies

Keywords

- Therapeutic
- Inflammation
 - Low blood pressure
 - CNS

Patent Status

Patent pending

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Inhibitors of Nitric Oxide Synthases Using Corrin Derivatives (VA Reference No. 05-141)

Novel use of corrin-related molecules for treatment of a variety of disease conditions including inflammation and low blood pressure

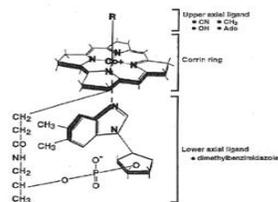
Technology

The Department of Veterans Affairs has developed a novel technology involving the use of cobalamins and other corrin-related molecules (similar in chemical structure to vitamin B12) to treat a variety of disease conditions (such as inflammation and low blood pressure) by inhibiting the action of nitric oxide synthases (NOS).

Description

Nitric oxide (NO) is a key biological messenger that is synthesized by the NOS enzymes: neuronal NOS (nNOS/NOS1), inducible NOS (iNOS/NOS2), and endothelial NOS (eNOS/NOS3). NO has multiple biological functions but has a primary role in relaxing the smooth muscle cells of the inner lining of blood vessels, thus dilating the artery and increasing blood flow.

Since misregulation of NO can play an important role in chronic and severe acute diseases, regulation of the NOS enzymes by drugs is an important objective of the pharmaceutical industry. Unfortunately, the structural similarity among the NOS enzymes makes them very difficult to target individually, while their prevalence throughout the body and their vastly different functions leaves little room for error in medical treatment. The inventors have demonstrated that cobalt-containing corrin derivatives directly inhibit NOS enzymes. The best candidates, hydroxocobalamin, cobinamide, and dicyanocobinamide, were the most potent inhibitors and were more active against nNOS than iNOS (and not against eNOS).



General Structure of Corrins/Cobalamins

Competitive Advantage

Unlike existing treatment methodologies, this invention:

- Is more potent in inhibiting nNOS and could be used to treat schizophrenia, depression, migraine headaches, and other neurological diseases.
- Also inhibits iNOS and could be used to treat septic shock (alleviating hypotension) and inflammation.
- Can be administered by multiple routes including orally, intramuscularly, or intravenously.

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).

