



Composition and Method for Treatment of Ischemic Neuronal Reperfusion Injury

Dantrolene can be used to protect against a nerve gas attack as it can be used to treat patients with ischemic neuronal reperfusion injury.

Contact

Hamid A. Bhatti
TreMonti Consulting, LLC.
2944 Hunters Mill Rd.,
Suite 204
Oakton, Va. 22124
(305)467-5942
hbhatti@tremonticonsulting.com

Dan McCabe
Associate General Counsel
Howard University
(202)806-2650
contracts@howard.edu

Inventors

Harpal S. Mangat MD
Pradeep Karla PhD

Potential Commercial Applications

- Ischemic Optic Neuropathy
- Ischemic Retinopathy
- Stroke
- Reperfusion injury after TPA treatment.
- Reperfusion injury after carotid endarterectomy.
- Chemical Warfare

Stage of Development

- The administration of dantrolene to treat two patients with optic ischemic neuropathy secondary to anesthesia.

Status

Seeking research collaboration & licensing partners

Background

What happens when an artery is blocked and the target organ is not receiving its blood supply? This is referred to as ischemia. Once the blockage is removed and blood starts to flow, this is referred to as reperfusion. One may think it is the ischemic phase which causes detrimental damage to the organ but in fact, synergistically, reperfusion has its own repercussions. There are a cascade of events which contribute to cell death, including, the accumulation of excitatory amino acids, intracellular calcium, arachidonic acid and other free fatty acids, hypoxanthine, xanthine oxidase, and platelet activating factor. It is the increase in intracellular calcium which is of particular interest to Dr. Mangat and colleagues. Calcium increases intracellularly due to dysfunction of a membrane pump which lets calcium out, increase in pump function which lets calcium in, and the final mechanism is during reperfusion, via the type 3 ryanodine receptor, intracellular calcium increases 30 times its current ischemic concentration.

Description of Technology

Dantrolene can be used to prevent or minimize neuronal cell damage that occurs during the reperfusion phase during reversal of an ischemic condition. It can be administered in various different ways but optimally it would need to avoid the first pass metabolism. Nerve gases have a similar mechanism of action of causing ischemic injury in the brain as does traumatic brain injury i.e. soman and v series nerve gases. Dantrolene alone cannot provide protection in such a situation but in combination with a residue of FMOC-valine, it can achieve the desired CNS penetration and protect against neuronal reperfusion injury seen in a nerve gas attack. The discovered formula can be administered by multiple routes but the desired route of administration is via inhalational/intranasal methods as current dantrolene preparations cannot be administered in these ways due to its harmful effects to the lungs. The mode of delivery would be via a gas mask or nebulizer. This strategy will prevent the detrimental rise of intracellular calcium causing neuronal cell death.

Opportunity

The method and compositions for the treatment of ischemic neuronal reperfusion injury is the subject of a patent application. Howard University is seeking a development partner to further characterize compound combinations, and to partner in initial human studies. Dr. Mangat and Karla are available to talk about the invention under a NDA.