PROPERTIES OF NBMI

Overview

NBMI is a chemical made of combining two natural ingredients identified as antioxidants. These are dicarboxylbenzoate and cysteamine. Benzoates are found in cranberries and other berries and have been used in the food industry even today as a major preservative due to their ability to scavenge reactive oxygen species and prevent food oxidation. Cysteamine, found in meat, is a by-product of the breakdown (decarboxylation) of the amino acid cysteine and is also found on the terminal end of CoEnzyme A.

Scientific Properties

Dicarboxylbenzoate has two negative charges on its two carboxyl groups. Cysteamine has one positive charge on its amino group. **By chemically combining one dicarboxylcarbonate with two cysteamines we produce an uncharged, hydropobic molecule with two reactive thiols attached as well as two nitrogens with exposed electron pairs that can change positions creating an "induced fit" for chelating exceptionally tightly several different toxic metals with thiol attracting chemistries.** Due to the chemistry in 2 above NBMI has biomembrane penetration properties that allow it, after digestion, to enter all the cells of the body including the blood brain barrier of the central nervous system (CNS) (IB, investigators brochure submitted to the FDA). The fact that NBMI does this has been established by using radioactive 14C-NBMI to measure the movement of NBMI in the body after ingestion using whole body autoradiography along with tissue removal and radiation analysis showing the levels of 14C-NBMI in all the cells of tissues of the body. What was observed is that 14C-NBMI peeks in the plasma at about 2-4 hours after ingestion and leaves the plasma to enter all cells of all tissues tested. It goes into different tissues at different levels and leaves all tissues to become non-detectable by autoradiography after 72 hours post ingestion. It did this in control rats and rats made toxic with mercury.

Published Studies/ Research

In our first published study (Clark et al. 2012) we demonstrated that excess **NBMI injected about 20 minutes after injection of 1 and 2 times the lethal dose of $HgCl_2$ prevented the observable toxicity and death of 100% of the animals.** At 14 times the lethal dose all animals were dead at 3-6 hours post injection of the $HgCl_2$ and none of the NMBI treated animals were dead at this time. After 48 hours about 1/3 the NBMI treated animals died but 2/3 totally recovered. Nothing else known can give this level of protection against mercury toxicity. The major observation of this study was that NBMI did not protect by transporting Hg^{2+} out of the body, but eliminated the toxicity by forming an inert and non-toxic Hg=NBMI complex. This was confirmed by synthesizing Hg=NBMI in the laboratory and testing it for toxic effects showing the NBMI bound mercury was non-toxic.

Oxidative Stress Reliever

Hg^{2+} induces oxidative stress or the production of hydroxyl free radicals that causes most of the tissue damage observed in this toxic state. Since Hg^{2+} is not a redox metal it cannot donate electrons to other molecules as occurs in the Fenton reaction that produces hydroxyl free radicals. This means that Hg^{2+} must displace either Fe^{2+} or Cu^{2+} which are the two major redox metals found in the body that can catalyze the production of hydroxyl free radicals. It known that Hg^{2+} displaces Fe^{2+} from the iron-sulfur centers of the mitochondrial electron transport system (ETS) rapidly inhibiting the synthesis of ATP and inducing oxidative stress by creating a supply of unbound Fe2+ to catalyze the Fenton chemistry production of hydroxyl free radicals from the O_2 rich mitochondrial matrix space using the superoxide anion (O_2^-) generated by the electron leakage increase caused by Hg^{2+} inhibition of the ETS. **EmeraMed has studies showing that NBMI binds and prevents hydroxyl free radical production catalyzed by both Fe^{2+} and Cu^{+} added to biological test systems.** Therefore, NBMI interferes with Hg^{2+} toxicity by (a) chelating it and preventing Hg^{2+} direct inhibition of enzymes/proteins by binding to their thiol (-SH) groups. (b) scavenging existing hydroxyl free radicals. and (c) also chelating displaced Fe^{2+} and Cu^{2+} preventing them from producing hydroxyl free radicals by Fenton chemistry and thereby eliminating the damaging oxidative stress induced by mercury cation.

It would be appropriate to indicate that all toxins that induce oxidative stress (e.g. bleomycin) do so by displacing Fe^{2+} or Cu^{2+} from naturally bound metal binding proteins. Oxidative stress is a common observation of most organic toxins. NBMI would eliminate the oxidative stress induced by these organic toxins by chelating the "unbound iron" that causes this toxicity (Patel et al. 2011)

The fact that NBMI binds Fe^{2+} much tighter than Fe^{3+} is likely why is it has been found safer than other iron chelators as Fe^{2+} is the free radical generator and Fe^{3+} is the most common native form of biologically bound iron (Cheng et al., 2022). The ability of NBMI to bind the two ionic forms of iron with vastly different affinities is most likely due to the built in "induced fit" properties of the NBMI chelation site where both the two thiols and two nitrogens can move and rotate to accompany the different coordination chemistries of the two ionic species (i.e. induced fit).

Safety Studies

NBMI has two properties that make it efficacious. One is its "induced fit" chelation abilities mentioned above that allow it to bind several toxic metals very tightly and the second is its ability to scavenge hydroxyl free radicals no matter the source of production. We have studies that show that NBMI is converted to NBMI-SO_3^- when exposed to a source of hydroxyl free radicals indicating that it scavenges 3 hydroxyl free radicals per NBMI molecule. This is supported by testing that shows NBMI has an exceptionally high ORAC (oxygen radical absorbance) score, especially for a product that can be taken orally (IB submitted to FDA).

Studies by other laboratories supported by EmeraMed has shown that **NBMI can lower the unbound iron levels in the CNS of genetically unbound iron test animals (H67D rats) and eliminate the oxidative stress in their brain tissue as well as the liver tissue** (Cheng et al. 2022). Also, NBMI can reduce the toxicity of lead exposure to brain cells better than the FDA approved product (DMSA) for this treatment (Gadde and Betharia, 2021). Again, the "induced fit" properties of the chelation site allow for exceptionally tight binding of lead (Pb^{2+}) **plus the ability to pass the biomembrane to enter the brain cell cytoplasm aids in the enhanced protection of NBMI.**

Phase II results of a study on Thalassemia show that NBMI can prevent the blood transfusion induced increase in ferritin levels in patients receiving regular blood transfusions and can do so without inducing toxic drug related adverse effects (Tanja Turk et al. Submitted to Lancet Journal 2022).

Phase II results of a small study on PD (MSA and PSP) showing the effects on these two forms of human neurological illness associated with increased unbound iron in the CNS showing positive trends. (publication in progress for submission and available)

In addition to the above we have several patents awarded and others under consideration that we can produce on interest.