



DRUG SHOWS PROMISE FOR TREATING COGNITIVE PROBLEMS AND INFLAMMATION IN GULF WAR ILLNESS

The compound, monosodium luminol, shown to improve cognitive and mood function and reduce inflammation in a Gulf War illness model

January 17, 2020

Article was originally published in [Vital Record News](#) from Texas A&M University Health Science Center and is republished here with permission

Gulf War illness, or GWI, previously called Gulf War syndrome, is a collection of medically unexplained chronic symptoms that [one-third of veterans who served in the first Gulf War](#) experience even now, nearly 30 years later. This condition is characterized by central nervous system impairments—including cognitive and memory problems, mood dysfunction, sleep disorders and chronic fatigue—

and systemic symptoms such as gastrointestinal problems and hypersensitive skin. With such a wide variety of symptoms, historically, experts have been unable to find a treatment for the illness. However, [Ashok Shetty, PhD](#), professor with the [Department of Molecular and Cellular Medicine](#) at the [Texas A&M College of Medicine](#) and associate director of the Institute for Regenerative Medicine, and his research team took a significant step forward with regard to treating this mysterious illness. [Their findings](#), a result of a study funded by the [Department of Defense](#), were recently published in [Redox Biology](#).

Modeling Gulf War illness

During the war, veterans were exposed to multiple chemicals. Although the exact cause of Gulf War illness is unknown, it is generally understood that [the combination](#) of [pyridostigmine bromide](#) (an anti-nerve agent used as a pretreatment to protect troops from an attack with nerve gas agent), DEET (a mosquito repellent) and permethrin (a pesticide sprayed on clothes to keep rodents and insects away) played a significant role.

“In our study, after administering the chemicals, the models presented Gulf War illness symptoms that closely resembled the symptoms veterans experience every day,” Shetty said. “They have memory problems, concentration issues and depressive-like behavior. Furthermore, the models experienced similar systemic problems and the blood samples showed elevated levels of proinflammatory cytokines.”

A [previous study by Shetty](#) showed proinflammatory cytokines—which, when in too great of a quantity can eventually deteriorate brain tissue and cause cognitive and mood problems—can be used as a reliable biomarker to determine the progression of the brain inflammation.

Oxidative stress, free radicals and Gulf War illness

Another previous study by Shetty showed that the brain experiences [increased oxidative stress](#) and inflammation when suffering from Gulf War illness. Oxidative stress, or [an accumulation of free radicals](#), can happen for a number of reasons.

“Most GWI-related chemicals are acetylcholinesterase inhibitors, which are known to induce hyperexcitability in neurons and cause inflammation,” Shetty explained. “These hyperexcited neurons are caused by an excess of free radicals.”

Free radicals are uncharged molecules with an unpaired electron. Therefore, Shetty looked toward an existing drug known to balance out the free radicals by bringing the body back to normal levels as a solution. Although not FDA-approved in the United States, [monosodium luminol](#) has been tested for use with cancer patients in Europe and Russia.

“The drug is a redox balancing drug, as it can donate and receive electrons. In other words, it maintains redox homeostasis, or an equilibrium of free radicals,” Shetty said. “When a shift in the balance of free radicals occurs, oxidative stress happens.”

Measuring the cognitive function

During the study, the research team administered the drug at different doses for several weeks. They measured the levels of oxidative stress, inflammation and cognitive function. Oxidative stress and inflammation can be quantitatively assessed through various markers in the body. However, cognitive function cannot.

To decrease the subjectivity of measuring cognitive function, the team used three tests. First, they tested the hippocampus via the object location test. This test investigates the ability to discern minor changes in the environment. The second test, called the pattern separation test, measures ability to distinguish similar, but not identical experiences. For the third test, the researchers conducted a depression test to measure the amount of depressive-like behavior in the models.

Monosodium luminol’s impact

All three of these tests measured common cognitive issues veterans with Gulf War illness experience: problems with working memory, memory recall and depression. As expected, the models had difficulty with all three tests. However, the models that

received the drug tested close to normal levels of cognitive function with all of these tests.

Similarly, the monosodium luminol brought the elevated oxidative stress and inflammation levels back within normal range. “We measured the oxidative stress markers in the blood and they were normalized,” Shetty said. The drug helped both the cognitive and systemic symptoms in the models of Gulf War illness.

“When you have inflamed conditions in the hippocampus, neurogenesis—the production of new neurons—goes down,” Shetty said. “We know people with [depression](#) and Gulf War illness have very low levels of neurogenesis. Low levels of neurogenesis are related to depression, problems in making new memory and cognition.” Shetty said neurogenesis actually increased in the models after taking this drug.

The next step

Presently, the drug is not approved by the U.S. Food and Drug Administration (FDA), but there is a pharmaceutical company conducting the required tests to get approval for monosodium luminol to be administered in the United States. Furthermore, the Department of Defense is backing several studies with this drug.

“From what we can tell right now, this drug does not seem to have any side effects,” Shetty said. “Theoretically, if this drug gets approved for use in the United States, this drug would need to be taken every day to maintain that redox homeostasis and, hopefully, be a solution for many of our veterans suffering from this illness.”

— Mary Leigh Meyer