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Researcher receives grant to study multiple sclerosis drug

by Vicky Cerino, UNMC public affairs

A UNMC College of Dentistry researcher has received a three-year, \$274,000 grant from the National Multiple Sclerosis Society to evaluate whether a drug well-known for its cholesterol-lowering effects may stop the destructive process of multiple sclerosis.

Kalipada Pahan, Ph.D., associate professor of biochemistry, is principal investigator of the grant that will evaluate the effect of Gemfibrozil on the disease process in mice models. The drug, also known as Lopid, is a safe and popular Food and Drug Administration (FDA)-approved drug that lowers cholesterol.



MS is thought to be an autoimmune disease that affects the central nervous system (CNS), which consists of the brain, spinal cord and the optic nerves. Surrounding and protecting the nerve fibers of the CNS is a fatty tissue called myelin, which helps nerve fibers conduct electrical impulses.

"When there's inflammation in the brain, nitric oxide is produced and destroys or damages myelin or the nerve fiber, affecting the ability of the nerves to conduct electrical impulses," Dr. Pahan said. "The result produces symptoms of MS. The drug inhibits the production of nitric oxide."

In earlier studies, Dr. Pahan showed gemfibrozil inhibits the expression of nitric oxide and the production of excessive nitric oxide in brain cells, suggesting that the drug may inhibit the disease process of MS.

"We hope the drug ultimately will be effective in people," he said. "We've already proven in the lab that the drug has an anti-

inflammatory property. Now we want to know if it works in mouse models." If the study is successful, Dr. Pahan said, researchers will pursue a clinical study in humans.

"So far, there's only one drug available. However, it is expensive and has a lot of side effects," he said. "It causes a reaction from a weekly injection and is only 30 to 40 percent effective in patients. Even if we can find a drug that's 50 percent less expensive and 50 percent more effective, that would be better."

Dr. Pahan's work focuses on studying a variety of anti-inflammatory drugs that might stop the MS disease process.

In the April issue of the *Journal of Immunology*, Dr. Pahan's research team published results showing sodium phenylacetate and sodium phenylbutyrate, two FDA-approved drugs for certain disorders in children, effectively block symptoms of the disease process of MS in mice.

"These two drugs are safe and have several advantages over interferon-b, the approved drug for MS," Dr. Pahan said. "These drugs are fairly nontoxic and less expensive compared to interferon-b. Instead of taking painful interferon injections, patients may be able to take these drugs orally by drinking water or milk."

Dr. Pahan said he is motivated to do research on multiple sclerosis because it affects people in the prime of life.

"This disease affects young people just starting their careers and family lives. There is no other disease in the world that specifically targets young people like this. This is the frustrating part of this disease," Dr. Pahan said.

Although the disease is not fatal, it causes weakness, tremors, loss of vision, cognitive changes, depression and other problems. Within 15 years of the onset of the disease about half of the patients become wheelchair bound. During the final stages of the disease, patients are bedridden. In Nebraska, about 110 to 140 cases per 100,000 people occur, according to the National Multiple Sclerosis Society. An estimated 1,600 to 1,800 Nebraskans have MS.

About 400,000 people in the United States have multiple sclerosis, which is often diagnosed between age 20 and 40, reports the National Multiple Sclerosis Society. It is more common among Caucasians, particularly those of northern European ancestry, and is more common in women than in men. Some of the potential causes of the disease are believed to be viruses, as well as environmental, genetic, and immune system factors.

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