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Research with Red Tide Toxin Yields Potential Therapies for Cystic Fibrosis

Researchers working with Florida red tide discovered two new compounds that may treat mucus build-up associated with cystic fibrosis and similar lung diseases. Preliminary studies show these compounds improve the flow of mucus through the respiratory tract, allowing airways to clear more quickly and efficiently.

"These compounds are excellent candidates for the development of an entirely new class of drugs targeted for the treatment of mucociliary disease," said Kenneth Olden, Ph.D., director of the National Institute of Environmental Health Sciences.

The NIEHS, one of the National Institutes of Health, provided \$6.6 million to scientists at the University of North Carolina at Wilmington and Mount Sinai Medical Center in Miami Beach for the study. The findings are published in the January issue of the *American Journal of Respiratory and Critical Care Medicine*.

Florida red tide consists of microscopic plant-like cells that produce a potent chemical toxin that causes fish kills, contaminates shellfish, and creates severe respiratory irritation in people. As the concentration of red tide increases, waves and wind disperse toxin particles into the air, causing irritation of the eyes, nose, throat, lips and tongue.

After identifying the most potent of the red tide toxins, researchers asked a second question: Can the respiratory problems caused by the toxin be prevented? Their research led to the discovery of two "anti-toxins" — a man-made compound known as β -Naphthoyl-brevetoxin, and brevenal, a natural compound produced by the organism itself. Experiments conducted in sheep revealed that both compounds were able to block the effects of the red tide toxin on the respiratory system.

While conducting experiments on the red tide anti-toxins, researchers made an even more important discovery — the anti-toxins behaved much like drugs used to treat cystic fibrosis. "We found these compounds are able to speed up the clearance of

mucus from the lungs," said Daniel Baden, Ph.D., director of University of North Carolina at Wilmington's Center for Marine Science and director of the project.

According to Baden, mucociliary clearance is one of the most important defense systems in the lungs, protecting the airways from bacteria and pollutants. "We think the ability of these anti-toxins to improve the clearance of mucus may be due to a combination of increased movement of the cilia, the tiny hair-like structures that line the airways, and a thinning of mucus," he said.

Tests conducted in experimental animals showed these compounds to be effective at doses 1 million times lower than the current medications used in the treatment of cystic fibrosis. "These agents can improve the clearance of mucus, and they may also work at concentrations that have no side effects," said William Abraham, Ph.D., a pulmonary pharmacologist at Mount Sinai Medical Center and author of the study.

"These compounds will serve as experimental models in the development of drug therapies for those who suffer from cystic fibrosis and other lung disorders characterized by excessive mucus secretion," said Baden.

Cystic fibrosis is the most common fatal genetic disease among Caucasians. Approximately 30,000 Americans have cystic fibrosis, and 12 million people carry the defective gene but are not affected by it. A person with cystic fibrosis produces thick, sticky mucus that provides a perfect breeding ground for bacterial growth. Cystic fibrosis patients are susceptible to more strains of bacteria than others, and have a much harder time fighting these infections.

Symptoms of cystic fibrosis include frequent wheezing, chronic cough, and pneumonia. While chest thumping is used to clear thick mucus from the lungs, medications can be given to thin the mucous and help breathing.



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