Sea Worms and Plants Spur New Drugs

Earth's seas and forests, some of nature's most productive chemical laboratories, continue to brew concoctions that hold promise as human medicines. By subtly modifying two obscure natural molecules — one from an ocean creature and one from a plant — scientists are developing potential new treatments for Alzheimer's disease, a degenerative brain condition that affects an estimated 5 million Americans over the age of 65.

William R. Kem, a chemist at the University of Florida, Gainesville, and his colleagues have synthesized from a neurotoxin found in marine worms a compound that ameliorates some symptoms of Alzheimer's disease. The compound, GTS-21, "acts in a way totally different from previously investigated drugs," Kem said this week at a meeting of the American Chemical Society in Anaheim, Calif. "It stimulates a particular type of site in the brain called the alpha 7-type nicotine receptor."

The brain has several varieties of nicotine receptors, which affect autonomic nervous system functions controlling blood circulation, digestion, and skeletal muscles. However, if scientists can stimulate the alpha 7 receptors without disturbing the other nicotine receptors, they may be able to enhance cognitive abilities without causing undesirable side effects.

Those effects, including high blood pressure, anxiety, and disturbance of heart rhythm, make nicotine itself an unsafe treatment for Alzheimer's patients.

Kem and his colleagues derived GTS-21 from anabaseine, a toxin used by nemertine worms to paralyze prey and deter predators. After synthesizing and testing more than 100 derivatives of the toxin over 8 years, Kem's team concluded that GTS-21 has the greatest potential as a drug for treating Alzheimer's disease in human beings.

As Alzheimer's progresses, nicotine receptors in the brain gradually disappear; half of them may have vanished by the time a patient dies. The GTS-21 compound aims to stimulate the surviving nicotine receptors and delay the onset of debilitating symptoms.

Although the drug does not cure Alzheimer's disease or repair underlying nerve damage, it does lessen neurological symptoms in laboratory animals. Tests of GTS-21 in rats showed boosts in memory and a slowing of nerve cell degeneration, Kem says. An animal trial to measure cognitive abilities found that old rabbits exposed to the new compound could learn almost as rapidly as young rabbits, reports Diana Woodruff-Pak at Temple University in Philadelphia.

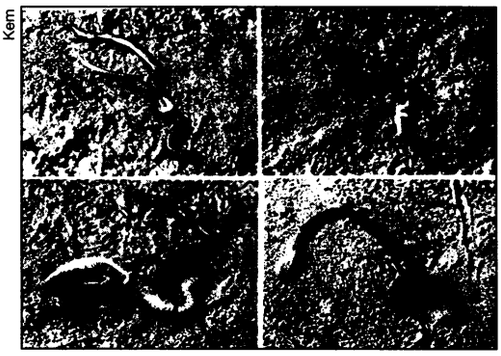
In humans, warding off the debilitating and life-threatening symptoms of Alzheimer's disease may help patients and their families cope with the condition's devastating effects. Delaying hospitalization by 6 months to a year could save billions of dollars in health care costs, Kem says. Clinical trials of GTS-21 will begin in late 1995.

Two other molecules that may help Alzheimer's patients come from the Caucasian snowdrop, a member of the *Amaryllidoidae* plant family. Raymond W. Kosley, a chemist at Hoechst-Roussel Pharmaceuticals in Somerville, N.J., and his coworkers derived the two compounds, P11012 and P11149, from galanthamine, an alkaloid substance found in the plant.

Since Alzheimer's patients tend to suffer from low concentrations of the neurotransmitter acetylcholine, the researchers looked for a compound that could diminish breakdown of this substance in the nervous system.

Both P11012 and P11149 achieved that goal in animals, mimicking the positive effects of the drug Tacrine, currently used to treat people with Alzheimer's disease. Users of Tacrine, however, can suffer liver damage. In Europe, some people with the neuromuscular disease myasthenia gravis are taking the new compounds, without reported liver damage.

In the United States, clinical trials of the new galanthamine derivatives may begin within a year, Kosley says. — *R. Lipkin*



Kem

Nemertines, small marine worms found under rocks in shallow seawater, paralyze their prey with the toxin anabaseine.

A sea surprise: Some corals dine vegetarian

Ocean dwellers would drive a chef nuts. Certain sponges, once considered the picture of happy herbivores, are actually crustacean-trapping carnivores, researchers found recently (SN: 2/4/95, p.69). Now, scientists say that some species of coral, long considered carnivores, prefer the vegetable plate.

"A . . . soft coral [*Dendronephthya hemprichi*] from the Red Sea feeds almost exclusively on phytoplankton, a mode of nutrition so far unknown for corals," report Katharina E. Fabricius of the University of Munich in Germany and her colleagues. Most corals survive on zooplankton, which is composed of tiny animals.

The scientists wondered how the common *D. hemprichi* manages to grow so well. Most corals play host to algae, which provide them with carbon, but *D. hemprichi* does not. So the researchers assessed the food preferences of this coral in their laboratory, they report in the April 7 SCIENCE.

They found that *D. hemprichi* consumed large quantities of phytoplankton fairly quickly. Indeed, phytoplankton supplied about twice as much carbon in *D. hemprichi*'s diet as zooplankton, which made up less than 1 percent of the food in its gut, says coauthor Yehuda Benayahu of Tel Aviv University in Ramat Aviv, Israel.

Carl Hansen/ Smithsonian Institution

A mix of stony and soft corals.

The scientists now know of three other coral species that dine primarily on phytoplankton, they report.

Corals trap their food on branched tentacles. Soft corals have closely spaced pinnules, or branches, on their tentacles that make them well suited for capturing phytoplankton, which are smaller than zooplankton, the authors note. What's more, soft corals have relatively poorly developed stinging cells on their tentacles, which makes it more difficult for them to prey on animals.

The herbivorous corals probably evolved to take advantage of an abundant food source not tapped by other species, Benayahu says. Researchers now want to find out how widespread this vegetarian movement is among reef dwellers.

In an unpublished study, Benayahu and his colleagues find that *D. hemprichi* reproduces all year, "which is completely exceptional within the coral reef," he says.

— *T. Adler*