



Harvesting the Shelves of Neptune's Pharmacy

BY KATHY HART

From Hawaii's rocky reefs to the pink sands of the Caribbean, scientists are turning to the sea to stock the pharmacies of the twenty-first century.

As they explore the Earth's final frontier, researchers are just beginning to probe the ocean and its biota for use in drugs, food additives, cosmetics, agriculture and other products.

Perhaps the ocean's greatest promise for the future, they believe, lies not in its role as the world's larder, but in its capacity to become the world's next pharmacy.

Our present pharmacy draws on terrestrial plants and herbs that have been dispensed for thousands of years.

Today's drugs are derived from land-based organisms or synthetic replicas. But the future for pharmaceuticals lies in one word: ocean. And researchers will have a wealth of plants and animals to test. Almost 80 percent of all the Earth's organisms live in the sea.

Ocean submersibles equipped with robotics are making it possible for researchers to dive deeper and linger longer in Neptune's domain. They are harvesting algae, corals, marine worms, seaweeds, sponges and countless other plants and animals for testing.

And coming from the watery environment makes marine plants and animals different—better able to fight diseases and viruses.

Already scientists have discovered marine-derived drugs active against viruses, cancer and maybe even AIDS.

Only a few marine drugs are on the market now, but others are under development and consideration for approval by the Food and Drug Administration, says Richard Moore, director of the Natural Products Program at the University of Hawaii.

And Sea Grant scientists from Hawaii to Puerto Rico are playing a role in the development of marine pharmaceuticals.

In laboratories in Washington and Delaware, Sea Grant researchers took a byproduct of seafood processing—discarded crab, shrimp, crawfish and lobster shells destined for the dump and turned them into materials fit for sutures and contact lenses.

Chitin (pronounced kite' in), the glue mollusks use to build their shells, possesses unique healing powers. And when converted into chitosan, a simple derivative that is non-allergenic, non-toxic and biodegradable, it becomes the stuff medicines will be made of.

Chitosan can be woven into bandages and sutures that promote quicker healing of wounds and burns with reduced scar tissue. It is molded into contact lenses that are used as dressings for eye wounds and surgery scars.

For transplant victims, chitosanmade blood vessels could reduce rejection of the transplanted organs. For burn patients, a chitosan film forms an artificial skin that could speed recovery. And for folks suffering from athlete's foot, a chitosan ointment could spell relief.

All of these chitin products are in advanced stages of development and testing. And even more are on the way.

University of Washington scientists are studying the use of chitin to repair severed nerves. But chitosan's biggest promise for the future may lie in its ability to lower cholesterol.

Chitin carries a strong positive charge, which means it acts as an attractant. If ingested, it's possible chitosan could act as an absorbent carrier that removes cholesterol from the body. It has already lowered cholesterol in animals without side effects. But General Mills, the company exploring chitosan's anti-cholesterol ability, has yet to test the derivative in humans.

But crab shell by-products aren't the only marine substances intriguing Sea Grant scientists. Delaware researchers are also delving into medical uses for mussel glue—a strong adhesive used by mussels and barnacles to attach themselves to rocks, piers and even each other.

This natural glue hardens and forms a strong adhesive bond in a watery environment that is not unlike the inside of the mouth, the eye or the human body.

A little dab of this non-toxic adhesive could revolutionize the way broken bones are set, eye surgery is performed and cavities are filled. Even soft body tissues and vital organs could be repaired with a drop or two of mussel glue.

But if arthritis is a nagging pain making you miserable, a sponge may offer comfort.

Hawaii Sea Grant scientists have isolated a substance called manoalide from a Pacific sponge. It promises to offer all the benefits of the commonly used anti-inflammatory drug hydrocortisone. But unlike hydrocortisone, it poses none of the side effects of steroids.

This anti-inflammatory snake oil presents a passel of medicinal uses: arthritis, auto-immune diseases, asthma, multiple sclerosis, therapy for organ transplants, skin diseases, attacks of poison oak or ivy, insect bites and, yes, snake bites.

An amino acid extracted from marine algae and bacteria by California Sea Grant scientists could aid in the diagnosis and treatment of nervous system disorders. And an acorn worm discovered in the deep waters off Maui by Hawaii researchers holds promise for treating tumors.

This exploration of the underwater pharmacy is not a lonely search. Researchers from marine institutes, pharmaceutical companies and national health organizations, such as the National Cancer Institute, are unlocking some pharmaceutical secrets, too.

Here are a few other noteworthy discoveries:

• An algae extract that stimulates the immune system could become important for AIDS and cancer patients.

• A sponge derivative has inhibited the AIDS virus in laboratory experiments.

• From a green slimy pancake that encrusts rocks and corals may come a new cancer drug. The drug also displays anti-viral tendencies that may make it useful in fighting yellow fever and herpes.

 Leukemia victims may see a cure in a marine coral.

But the discovery of these marine drugs and their possible production raises the spectre of overharvesting, exploitation and possibly extinction of marine animals and plants.

But this may not happen, says Moore, a Sea Grant scientist at the University of Hawaii.

Moore says that for now the ocean presents too many obstacles to make massive harvesting economically feasible. But, he says, other options are available.

Some organisms and plants could be cultured, creating a constant supply for production. Others could be chemically synthesized or engineered using biotechnology.

However they make it to the pharmacy shelves, marine drugs are a wave of the future.



Horseshoe Crabs Become Blue Blood Donors

leave a pharmaceutical company without this standard test.

Limulus amoebocyte lysate, the star of this industry, is a derivative of the horseshoe crab's blood, which can be extracted with no apparent harm to the animal.

BY CARLA BURGESS

"We take a sample of their blood, give them a little donut and a glass of orange juice and they go back in the water," Jim Finn says jokingly.

Finn, owner of Finn-Tech Industries Inc., bleeds 200 to 300 of the larger female crabs per week at the Delaware Bay laboratory.

The horseshoe crab is placed in a rack, flexed by the hinge joining its abdomen and head. A hypodermic needle is then inserted into the animal's heart chamber for the donation, which can comprise up to 30 percent of its blood.

The blood—bluish in color because of a copper-containing pigment that functions in respiration—

Up north it's been touted as "New England's original blue blood." But the horseshoe crab medically important as it is hasn't always been held in royal esteem.

With its voracious appetite for shellfish and tendency to tangle with fish-filled nets, the horseshoe crab is considered a pest by many shrimpers and shellfishermen.

In response to a 1950s bounty on the animals, Cape Cod children earned five cents apiece from the Commonwealth for every crab tail turned in. Along the Delaware Bay, crabs were slaughtered by the hundreds of thousands and ground up for fertilizer.

During this same time, a scientist was quietly discovering how the animal's blue blood clots to kill invading bacteria.

Frederik Bang's discovery would eventually lead to a superior test for deadly impurities in pharmaceuticals and an important new medical industry. Today, no drugs is centrifuged to separate the amoebocyte, or blood cell, from the plasma. The freeze-dried product of the cells is used in the lysate test.

"This is an in vitro test for feverproducing subtances that are found in drugs or devices," Finn says.

At more than \$15,000 a quart, lysate is still more cost-efficient than its predecessor. It replaces the more cumbersome, expensive and less sensitive rabbit test, in which test solution was injected into the bloodstream of a live rabbit.

The animal was subsequently monitored for fever, shock or death. Drugs causing even a fever in rabbits were rejected.

The lysate test is a simple one, in which a small amount of the lysate reagent is mixed with an equal part of the solution to be tested. After about an hour of incubation at body temperature, the mixture is examined. A clot indicates the presence of bacteria.

The case of the tainted swine flu vaccine in 1976 apparently resolved the rabbit-versus-crab debate. The lysate test, the sole detector of the deadly endotoxins in some of the vaccine, emerged the victor.

Following that incident, the FDA provided guidelines for use of lysate in testing drugs, blood products, intravenous fluids and medical devices such as syringes.

In addition to these uses, research continues into lysate's clinical applications.

Lysate's use as a diagnostic tool for bacterial diseases has been limited by its inability to differentiate between species of bacterial toxins. This distinction is necessary for prescribing antibiotic therapy.

Still lysate has contributed to diagnoses of many diseases, including spinal meningitis, urinary tract infections and gonorrhea. Carl Shuster, adjunct professor at the Virginia Institute of Marine Science and a pioneer of horseshoe crab research, is building a library about the animal at the school.

In evidence of the rapid research strides made since its introduction, Shuster says information on lysate work alone nearly equals that on the animal's history.

And when you talk horseshoe crabs, you're talking history. Hundreds of millions of years of it.

The earliest ancestor of the horseshoe crab, the aglaspids, swam the waters 500 million years ago.

The horseshoe crab is really not a crab at all. It's a member of the same phylum as crabs arthropod—but is most closely related to spiders and scorpions.

The animal has three segments: the head and chest region, covered by a hard shell or exoskeleton; the abdomen, carrying its six pairs of appendages; and its spiny tail or telson, used for leverage.

The horseshoe crab's eyes are also medically important. Much of what we know about human vision has stemmed from research on the animal's large compound eyes and long optic nerve.

One must wonder about the animal's chance of survival amid

the demand and virtual requirement for its blood.

"There's no doubt we've got to start getting a serious handle on population dynamics," says Shuster, but he noted that laboratory bleeding is not to blame for high mortality. "The biggest impact is when they take them for fisheries, cutting them up for eel bait and conch bait."

Experts believe that laboratory bleeding does not significantly increase horseshoe crab mortality. And crabs can regain their blood volume in three to seven days, though it takes months to regenerate amoebocytes.

A study by Anne Rudloe in the early 1980s, in which 10,000 crabs were tagged and half were bled, revealed a 10 to 11 percent increase in mortality among bled crabs.

"Crabs have been found two years after being bled breeding on beaches," says Finn, who is involved in a tagging program with Shuster to learn more about the animal.

The horseshoe crab has coexisted all these years in a "soup" of aquatic bacteria and toxins. The reaction of its blood to invading bacteria suggests a sort of primitive immune system that has helped the animal—and mankind to survive.



Sharks: Resisting Cancer Naturally

Just when you thought it was safe to go back in the laboratory ... scientists are in there studying sharks and their potential value in cancer treatment.

The creatures appear to have a natural resistance to cancer.

"You just don't find sharks with disease, generally," says Carl Luer, a marine biochemist at Mote Marine Laboratory in Florida.

A good bit of his work there involves exposing sharks, skates and rays to potent chemical carcinogens.

"We haven't been able to produce anything to even look like the early stage of a tumor," Luer says.

Exposure during even the initial stages of the embryo, an especially vulnerable period, has failed to produce a tumor.

Jay Grimes, director of New Hampshire Sea Grant and a professor at the University of New Hampshire, has studied bacteria associated with shark tissue or cartilage.

"All tissue in healthy sharks, with the exception of blood, are heavily colonized by a variety of bacteria," he said. "But these bacteria do not cause disease in the shark. "The bacteria is apparently living in a symbiotic relationship we don't understand yet," he says, noting the animal appears affected only in the case of undue stress.

Shark cartilage protein, Grimes explains, appears to have antineoplastic qualities, meaning it inhibits the growth of tumors.

Other research has shown that injections of the cartilage extract have dried up the blood vessels in cancerous tumors of laboratory rats.

This potential cancer treatment stems from scientists' attempts to inhibit the growth of blood vessels that feed tumors.

According to a Massachusetts Institute of Technology report, extract from calf cartilage also inhibits blood vessel growth. But for extensive experiments, it's hard to get enough extract from the bonerich skeletons of mammals.

BY CARLA BURGESS

Shark skeletons, on the other hand, are all cartilage.

Apparently, the research on sharks and cancer is still in its formative stages.

"The hard part is to keep funded," says Luer.

He hopes various institutions can eventually work together to advance the research on shark cartilage protein.

Luer adds that a treatment, when all the bugs are worked out, should be synthesized.

"We're not looking to rape the environment of all sharks simply to produce this product," he says. "There just aren't enough sharks to support this kind of thing."

The Back Page

"The Back Page" is an update on Sea Grant activities—on research, marine education and advisory services. It's also a good place to find out about meetings, workshops and new publications. For more information on any of the projects described, contact the Sea Grant offices in Raleigh (919/737-2454). For copies of publications, write UNC Sea Grant, Box 8605, NCSU, Raleigh, N.C. 27695-8605.



Fisheries enforcement officials along the East Coast are clamping down on the soaking of sea scallops.

By immersing sea scallop meats in water for several hours, the edible abductor muscle inflates, says Sea Grant's seafood specialist David Green.

Why swell a sea scallop?

Northeast sea scallops have been overharvested, and the mollusks netted are often small. Too small, in fact, to meet the minimum harvest sizes imposed by the New England Fishery Management Council.

To dodge size limitations, some fishermen and processors are steeping the scallops to inflate their size. But the dunking is illegal in most East Coast states, including North Carolina.

A Massachusetts processor was shut down and 1,500 pounds of sea scallops were confiscated because the plant was handling soaked scallops. Enforcement officials with the N.C. Division of Marine Fisheries are also monitoring Tar Heel plants that frequently process sea scallops.

Green says processors and fishermen should be aware of the regulations about soaking.

But, he adds, the soaked mollusks do not pose any health risk to the public. The added water will only make the scallops splatter more in the frying pan.

If seafood specialist David Green has anything to do with it, crayfish will no longer be just a Louisiana commodity. Green has been working with Pamlico County seafood processor Tom Caroon to develop a processing procedure for the Bayou crustacean.

He's worked out handling methods that will meet sanitation standards and processing time temperatures. With this information, Tom Thumb Seafood can now handle as much as 1,000 pounds of crayfish a day.

Handling crayfish may help crab processors extend their work season. Crayfish are harvested from mid-March until early June, but blue crab season doesn't peak until July.

And Green says that plants which are certified as crustacean plants by the N.C. Division of Shellfish Sanitation can process crayfish with their existing equipment and a few modifications.

Green has also been looking into canning and pickling the crustaceans.

For more information about processing crayfish, call Green at 919/726-7341.



munities in April by a Duke University geologist.

He says the "best and worst" list of 25 coastal communities is oversimplified and could lead those shopping for coastal real estate to make unwise decisions.

The list, compiled by Orrin Pilkey Jr., a Duke University geologist, and Todd Miller, executive director of the N.C. Coastal Federation, ranked communities according to the natural characteristics, anticipated development and physical changes, quality of management and potential danger to people.

But Rogers says the rankings overgeneralize the safety of a site by comparing large sections of shoreline.

"You can't categorize a community or island by the level of risk on part of the island," Rogers says. "You have to be site specific." According to Pilkey's scorecard, Brunswick County's Sunset Beach was rated the safest coastal community; North Topsail Shores in Onslow County, the riskiest.

Sunset Beach earned Pilkey's accolades because its beaches are accreting instead of eroding. But Rogers says that hasn't always been the case.

Sunset Beach has had periods when the island lost 25 feet of sand per year, he says. A new inlet was cut in the southwest end during Hurricane Hazel in 1954, and parts of the northeast end have been open water as recently as the late 1960s.

And Rogers questioned the reliability of Sunset Beach's floating bridge if storm evacuation became necessary.

In contrast, Rogers says some areas near the bridge at North Topsail Shores, the community rated as worst, have low erosion rates and good access to the mainland in case of evacuation.

"Some of the best sites at North Topsail Shores would be a far better choice for a home than a bad site at Sunset Beach," Rogers says.

And when it comes to evacuation, Ocracoke, the second "safest" community on Pilkey's list, can be hard to leave behind. Ocracoke is accessible by a ferry system that must shut down when winds exceed 35 to 40 knots.

The third slot on Pilkey's safety list was occupied by Nags Head—site of some of the worst erosion on the North Carolina coast in recent years, Rogers says.

Rogers and Pilkey agree that prospective coastal homeowners should fully realize the risk of buying property in one of nature's most dynamic, changeable systems. But Rogers believes buyers should look beyond communities to specific sites.

For more information about choosing coastal real estate, send for a copy of Your Place at the Beach: A Guide to Buying Vacation Real Estate. Ask for UNC-SG-87-04. The cost is \$2.50.

If you have further questions, call Rogers at 919/458-5498. Or write P.O. Box 130, Kure Beach, N.C. 27889.

Coastwatch

Coastwatch is a free newsletter. If you'd like to be added to the mailing list, fill out this form and send it to Sea Grant, Box 8605, NCSU, Raleigh, N.C. 27695-8605.

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Pass the word!

Big Sweep '90 is looking for zone captains to help coordinate the annual statewide cleanup September 22.

Zone captains help regional coordinators with publicity, recruiting volunteers and overseeing cleanup on the big day.

If your church, school, workplace or civic group would like to spearhead a group cleanup somewhere, let us know. This is one time when dropping a name is acceptable!

Call us at Sea Grant with your suggestions. Our number is 919/737-2454.

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105 1911 Building Box 8605 North Carolina State University Raleigh, NC 27695-8605

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