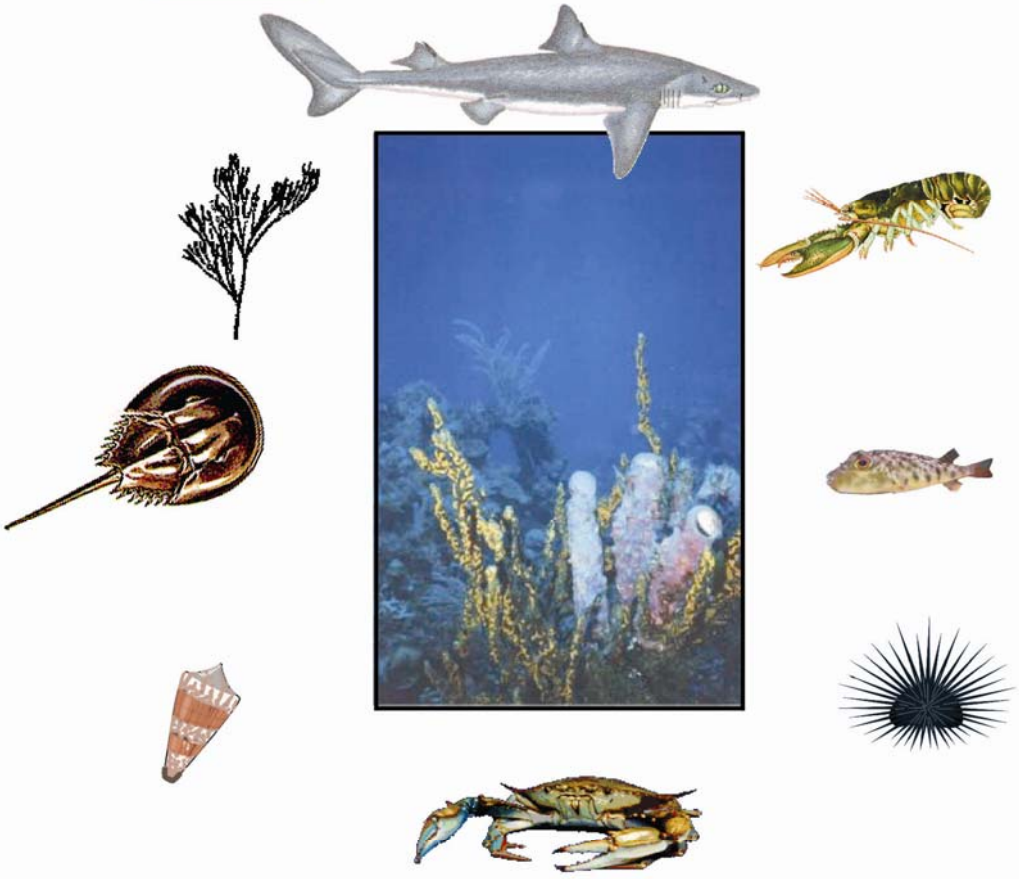
National Science Teachers Association
Dallas, Texas
March 31 - April 3, 2005

Medicines of the Sea



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Finding Medicines from the Ocean
Instructions for Teachers

Scientists are always looking for new medicines to cure diseases, stop pain, mend tissues, and kill infections. For years we have obtained drugs from organisms on land. More recently, explorations for new medications have led us to the oceans.

Finding new cures happens in steps.
Step 1. Scientists seek to find organisms with compounds inside of them that may have potential medicinal uses. This is a pretty big task. Where would you begin to look in the gigantic oceans? Scientists have found many of these compounds inside benthic invertebrates such as sponges, mollusks, tunicates, bryozoans, and soft corals. It may be that such animals rely on chemicals for defense. Sessile organisms may secrete substances to ward off potential competitors for space and food.
Step 2. Once you find a compound, how do you get enough for all the people who need this medication? Several methods are used. What works for one might not be feasible for another.

Harvesting – Collection of organisms is typically not the best approach. Populations could become depleted. Sometimes the compound can be extracted and the animal released. This would help sustain the providing organism's population.

Synthesis – Some compounds can be artificially made in large quantities by pharmaceutical companies. If they have no success making the actual molecular substance, they may be able to make something similar enough so that it provides the same results when used medicinally. This alternative molecule is not an exact copy of the compound found in the organism but it's so structurally similar that it will accomplish the same job as the original.

Cultures – Sometimes it is discovered that the animal you think is making the compound really isn't. Another organism living inside the animal you found might make it. Its manufacturer could be a small alga, for example. If companies can raise these algae in large amounts, then mass production of the compound is possible. Other examples of cultures also exist. Discoveries in horseshoe crabs have shown that the gill flaps produce the blood cells responsible for clotting when in contact with many disease-causing bacteria. These cells can be grown in cultures using the gill flaps.

Mariculture - Some marine species can be farmed so that many individuals are produced. The life requirements differ between animals making some easier to be raised on a farm than others. If it is successful, the compound in abundance can then be harvested.

The activity below is designed to be a GENERIC scenario. It is not intended to represent any specific health problem but instead to illustrate the basic steps in finding medicines from the sea.

Materials Needed: (Be creative in representing the animals below. You may use a specimen or make a puppet, cut out a picture, draw one, etc.)

- sponge
- bryozoan
- soft coral (like a sea fan)
- crab

- ✷ fish
- ✷ puzzle pieces cut from foam sheets (see patterns)
- ✷ small labeled boxes representing the different methods of mass production (harvest, synthesis, mariculture)

Directions:

1. Before students arrive, place puzzle pieces under "collected animals." Only one of the animals should have the "cure molecule." Some may have the other puzzle pieces that could be potential medicines even though they don't work (fit with the target molecule) for this scenario. You may want to select animals in which scientists have commonly found potential medicines. Other animals may not have any of the pieces. Fill the "Synthesis" box with ***cure molecule*** puzzle pieces. Leave the "Harvest" and "Mariculture" boxes empty to represent that these methods are not successful in producing large amounts of this compound in this given scenario.

2. Introduce the students to the generic scenario. A certain type of bacterium is causing some people to get sick. Inside it is a molecule (see representative puzzle piece) that helps this germ multiply so that the infected individual gets sick and may even die. We will call this molecule the ***target molecule***. This bacterium will replicate itself every time the ***target molecule*** joins with the ***multiplier molecule*** also found inside of it. If we can find a ***cure molecule*** that will attach to the ***target molecule*** and prevent it from joining with **the *multiplier***, we can stop the spread of the bacteria within the person.

3. Tell students to look in/under all the animals to find a puzzle piece that will join with the ***target molecule***. Ask the students in what animals they found the various pieces and how many are cure molecules. Discuss ideas of why so many medicines are found in these types of animals.

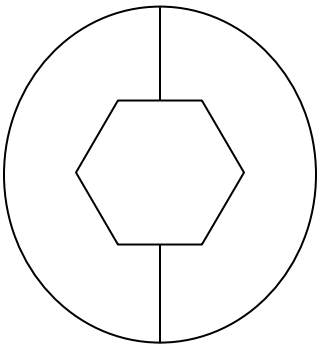
4. Ask students if they can think of ways to get enough of the ***cure molecule*** for all the many people who will need it. Instruct them to look in the boxes. Which method has produced a significant amount of the medicine? Discuss why "Synthesis" may be a possible production method. Discuss why "Harvesting" and "Mariculture" may have complications.

Other Ideas: Keep in mind that this is one of many possible scenarios you could use. You might have different scenarios represented throughout the class. One group's compound might be easily produced by synthesis with another's more successfully produced by mariculture, and so on. Also keep in mind that a symbiotic organism living in the collected specimen might be that actual producer of the chemical. You would introduce a "Culture" Box to your choices. Students could research different medicines from the sea and design the puzzle pieces / scenarios to teach the rest of the class about real life "cure molecules."

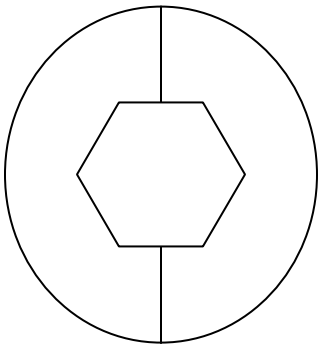
Resources

How Stuff Works web site.
http://www.howstuffworks.com/index.htm

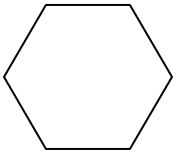
Pomponi, Shirley. 2003. Aquaculture & Cell Culture: Developing Techniques for Supply of Marine-Derived Drugs. NOAA Ocean Explorer: Deep Sea Medicines 2003 web site.
http://oceanexplorer.noaa.gov/explorations/03bio/logs/sept15/sept15.html



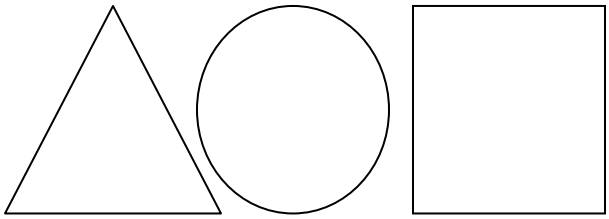
Target Molecule



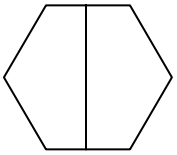
Multiplier Molecule



Cure Molecule



Potential Medicines



Synthetic Alternative Molecule

MEDICINES OF THE SEA 2005

ALGAE

http://chapmanlab.lsu.edu/digitalalgae/GulfAlgae/MMSBiotech.html

Sample of algae collected from Gas rig legs in the Gulf of Mexico, Louisiana area, that show pharmaceutical potential:
Agar Producer: *Gelidium* spp.
Antibacterial: *Cladophora* spp., *Centroceras clavulatum, Gelidium* spp.
Antifungal: *Bryopsis* spp., *Cladophora* spp., *Centroceras clavulatum, Gelidium pusillum, Jania* spp.
Antiherpetic: *Chaetomorpha* spp., *Cladophora* spp., *Enteromorpha* spp., *Ulva fasciata, Centroceras clavulatum*
Anti-inflammatory: *Gelidium* spp.
Anti-influenza: *Ceramium* spp., *Gelidium* spp.
Antitumoral: *Bryopsis* spp., *Chaetomorpha* spp., *Enteromorpha* spp.
Antiviral: *Bryopsis* spp., *Chaetomorpha* spp., *Cladophora* spp., *Enteromorpha* spp., *Ulva fasciata, Centroceras clavulatum, Gelidium* spp.
Differentiation of Leukemia or Melanoma Cells: *Ceramium* spp., *Gelidium* spp.
Diuretic: *Enteromorpha* spp.
Additionally, studies have shown that agar produced from red algae have **antirheumatic** properties and alginates from brown algae (Phaeophyceae) have been studied for **spinal chord, bone, and nerve regeneration; dermal repair, and as mucoadhesives**. *Spirulina* (Cyanophyta) is sold as a **nutritional** additive.

MUSSELS

http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=427802

Mussels produce and secrete specialized adhesives that function in water, allowing them to attach themselves in marine environments, which are characterized by salinity, humidity, tides, turbulence, and waves. They adhere tightly to surfaces underwater by using the byssus secreted from their foot. The byssus consists of a bundle of threads; at the end of each thread is an adhesive plaque containing a water-resistant glue that enables the plaque to anchor to wet solid surfaces. This strong and water-insoluble adhesion has attracted interest for potential use in biotechnological applications. Mussel adhesive proteins are able to form not only permanent and strong but also flexible underwater bonds to substrates such as glass, Teflon, metal, and plastic. Moreover, their biodegradable properties make them environmentally friendly. Mussel adhesive proteins can also be used as medical adhesives since they are nontoxic to the human body and do not impose immunogenicity.

CHITIN

http://www.ocean.udel.edu/horseshoecrab/Research/chitin.html

Chitin is natural, non-toxic, non-allergenic, anti-microbial, and biodegradable. It has a strong positive charge, which allows it to bind with negatively charged surfaces or materials, including metals, skin, and macromolecules such as proteins.

In the mid-1970s environmental regulations were passed to limit the dumping of untreated shellfish wastes in coastal waters, thus making the processing of chitin from shellfish waste an economical way to comply with the regulations and dispose of the thousands of tons of shellfish waste produced annually. Today, nearly 200 patents have been issued in the United States, in addition to those issued in several other countries worldwide, and there are nearly 15 major processors of chitin and chitosan around the world.

Early on it was found that chitin had wound-healing properties. By the mid-1950s, chitin-coated sutures were being used, which enhanced healing time by 35 to 50%. In the 1970s, researchers with the University of Delaware Sea Grant College Program developed a method to spin pure chitin filaments. These new chitin sutures could be absorbed by the body, eliminating the need for surgical removal. A Japanese firm bought the patent rights, and suture materials are now manufactured in Japan. In addition, this firm uses chitin to make dressings for burns, surface wounds, and skin-graft donor sites, which dramatically accelerate healing and reduce pain compared to standard treatments where the dressings must be removed.

Other medical uses for chitin include anti-bacterial sponges and hospital dressings, artificial blood vessels, contact lenses, tumor inhibition, dental plaque inhibition, and blood cholesterol control. Household products include sponges, diapers, feminine napkins, and tampons.

Make-up powder; nail polish; moisturizers; face, hand, and body creams; and toothpaste are just a few consumer products that might contain chitin.

Chitin is added to commercial feed mixtures containing whey, a by-product of the cheese industry. Many animals find it hard to digest the high-lactose whey. But chitin supports the growth of beneficial microorganisms in the animals' digestive tract — these bacteria produce enzymes that help the animals digest whey.

SEA URCHINS

http://www.msi.ucsb.edu/msilinks/mbc/mbctexts/mbc.htm

Another area of research in which marine organisms have provided new information is in the area of fertilization; this fundamental biological process is easily studied using sea urchins, an abundant coastal California organism. Research in this area has led to the discovery of the molecules on the surface of the sperm and egg that are responsible for gamete recognition and that may initiate development. This research impacts on design of contraceptives in mammals and has important implications for understanding cancer in terms of understanding how cell divisions are initiated.

CORAL

http://www.usm.my/r&d/frontiers/f2/3.html

December 2002
Coral is an alternative to creating bone replacements without using bovine or porcine bones that is natural, and disease-free.

The first phase of human testing was with 18 dental patients who underwent coral grafting when they had their tooth extracted. The results were encouraging, as the corals were found to stop bleeding, reduce swelling and promote healing of the wounded area.

Environmental lovers need not worry, as the team has the backing of experts at the Borneo Marine Science Institute, the biggest marine research institute in the country, which verified that that the amount of corals needed to make bones has negligible effects on marine life.

SPONGES

http://www.ftns.wau.nl/prock/Research/Rene/Dissertations/Sipkema.htm

It is estimated that approximately 15,000 species exist and in almost every species screened, one or more potential medicinal compounds have been discovered. These compounds possess anticancer, antiviral, anti-inflammatory, anti-malarial or antibiotic activities.

CONE SNAILS

http://www.docguide.com/news/content.nsf/news/8525697700573E1885256F79005C690C

NEW YORK, NY -- December 29, 2004
The FDA just approved a new analgesic called Prialt, or ziconotide intrathecal infusion.

Prialt, the man-made equivalent of a conopeptide found in the venom of the Conus magus snail, has been shown in recent clinical studies to be effective in reducing pain for patients that had failed all other therapies. Some examples of severe chronic pain sufferers are those with failed back surgery, injury, accident, cancer, AIDS, and other nervous system disorders. For more information on severe chronic pain or Prialt, consult your physician or visit http://www.prialt.com.

BRYOZOAN

http://scrippsnews.ucsd.edu/article_detail.cfm?article_num=661

Certain marine invertebrates such as *Bugula neritina*, a brown bryozoan animal with stringy tufts, live in a symbiotic relationship with bacteria that act as a chemical defense mechanism for the host animal.

In 2001, Professor Margo Haygood and other scientists in her Scripps laboratory found that such bacteria living in *Bugula neritina* were the source of bryostatins, a family of chemical compounds being closely studied for their potential as anticancer pharmaceuticals in leukemia, lymphoma and several cancers including colon, breast, ovarian and prostate.

DOGFISH SHARK

http://www.cancerchoices.com/squalamine.htm
A substance called squalamine found in the shark's liver suppresses the formation of new blood vessels in solid tumors, and may therefore, be useful in halting tumor growth.

Squalamine is currently being evaluated in Phase II clinical studies for the treatment of lung cancer, NSCLC, ovarian cancer, breast cancer, brain cancer, and other advanced cancers.

Since 1994, with funding from Magainin and the National Cancer Institute, Henry Brem, M.D., director of neurosurgical oncology and his co-researchers have been studying squalamine's anti-angiogenic properties. "The more we've explored this product , the better we like it." So far, they have learned three important things:

- Squalamine has proved to be non-toxic and a potent inhibitor of angiogenesis (tumors develop circulatory networks to nourish themselves, a process called angiogenesis) in animal models.
- It appears to be extraordinarily selective, halting only the growth of cells being stimulated by growth factors secreted by tumors.
- And, finally, it doesn't break down during digestion.

ABALONE

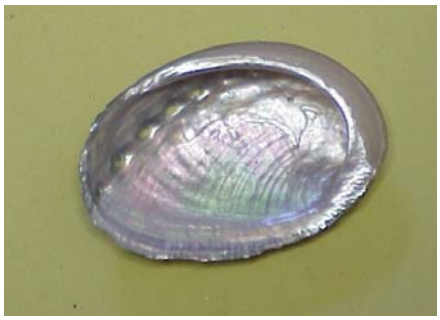
Scientists have cloned the abalone genes that are turned on and off during the process of Programmed Cell Death, and discovered a specific enzyme responsible for the snail’s Programmed Cell Death. Human diseases like Parkinson’s, Alzheimer’s, and Muscular Dystrophy occur when Programmed Cell Death fails.

ASSORTED

http://www.aibs.org/bioscience/bioscience-archive/vol46/apr.96.burris.html

Applying modern techniques to the study of marine organisms should not only tell us about the oceans and give us valuable products and processes but also enable us to expand the use of marine organisms as models for biological and biomedical research. The **squid** and its giant nerve axon already have told us much of what we know about nerve transmission, while the eye of the **horseshoe crab** has revealed many of the mysteries of vision. The **surf clam** is now used extensively to study the cell cycle and its control, and the **toadfish** provides a superb model for studying the mechanisms of balance control. The **sea urchin** continues to be a key model for learning about the molecular and cellular bases of reproduction and development, while the **shark** and the **skate** have taught us about both immunology and vision.

MEDICINES OF THE SEA



Dauphin Island Sea Lab

Joan R. Turner

Center for Excellence in Biomedical & Marine Biotechnology

BOCA COMPANY DEVELOPS MEDICINES FROM MARINE LIFE

by Stephen Pounds - Palm Beach Post Staff Writer

Dec. 27, 2004

BOCA RATON - Russ Kerr seems perfect to father the first U.S. medicine from marine life.

The Stanford-educated research professor lived on a sailboat off Fort Lauderdale until his family outgrew it. His office walls are cluttered with pictures from ocean expeditions. He even dresses the part, wearing a lime- and forest-green Hawaiian shirt as he patrols his laboratory at Florida Atlantic University.

Kerr has one foot in academia and the other in free enterprise. He is the director of FAU's Center for Excellence in Biomedical and Marine Biotechnology and chief science officer of Tequesta Marine Biosciences in Boca Raton, the first company to work jointly with The Scripps Research Center's Florida operation.

The drug-making genes discovered in his lab will be cloned to make synthetic equivalents for commercial drugs to treat herpes zoster, a type of chickenpox that causes a painful rash, and seborrheic dermatitis, a scalp condition that causes red, itchy scaling. There are treatments for both, but they are often inadequate.

During the past 80 years, scientists have looked to the land rather than the sea for new medicines. They have honed production methods for terrestrial drugs such as Taxol, a cancer treatment originally derived from the bark of the yew tree.

Only two companies — one in Spain, the other in Ireland — are close to producing ocean-derived drugs. Kerr and his partners want to make Tequesta Marine the third.

"We need people to find marine Taxols," Kerr said. "Only in the past 10 years has it become clear that we have a supply problem of drugs from nature."

The predicament is this: Reefs rich in live coral and sponges are disappearing and must be protected from further destruction by divers and boaters. If new medicines are to be developed from the ocean, they will have to come from molecular biologists and synthetic chemists who create copies of the real thing.

"Ultimately what we want are the genes. That's what's you use to create a synthetic drug," Kerr said.

Key step: FDA approval

More than 20 graduate and postdoctoral researchers in Kerr's lab huddle over beakers and high-tech testing equipment to unlock the secrets of the sea.

Researchers start with a clipping of live coral, flash-frozen directly from the ocean to preserve its chemistry. Once in the lab, the coral is thawed before students begin to separate the proteins inside. As many as 500 proteins might make up one slice of coral, but Kerr's researchers are interested only in ones that go into anti-inflammatory drugs.

"We're trying to isolate certain compounds... to find their chemical properties," said Jamie Frenz, a doctoral candidate working in the lab.

After proteins are extracted from the coral, a special device that operates at 2 degrees Fahrenheit painstakingly separates a protein into amino-acid sequences. Those sequences help to identify the right gene for a new drug. In the final

stage at FAU, genes are cloned for drug production.

Once we find something interesting, we put the gene in a bacteria and it produces it really fast and in large quantities," FAU postdoctoral researcher Lory Santiago said. "It's like a mini-factory."

After key chemical compounds are cloned in larger quantities, they'll be handed over to Scripps synthetic chemists led by K.C. Nicolaou, chairman of Scripps' chemistry department. Nicolaou's team will induce a number of chemical reactions to complete the drug.

Nicolaou, who was unavailable for an interview, has co-founded three companies. He is a member of the National Academy of Sciences, and his work has resulted in 79 patent applications, with 56 granted and 23 pending.

Tequesta Marine's first product will come from a molecule produced from marine micro-algae that one now-defunct biotech firm already tried to commercialize.

It went through early clinical human trials as an anti-inflammatory treatment, but it will need more trials and government approval before Tequesta can sell it.

The company can sell the drug as an anti-allergy additive in skin creams once it perfects the production method. Still, it's seeking $1 million to complete development as a medicine.

It hopes to approach the Food and Drug Administration about testing it on animals in the next 12 to 18 months.

"If you study the reasons that drug studies fail, it's when the FDA says, 'We don't think this animal study is relevant,' " said Tequesta Marine Chief Executive Rhys Williams, a former venture capitalist and combat diver.

In the meantime, Kerr's labmates search the waters off Fort Lauderdale and the Bahamas for coral while they hone the cloning process.

"The key to this is the cloning," Kerr said. "We're duplicating this protein in the bacteria, but it is precisely what happens in the coral."

FDA Approves Prialt (Ziconotide Intrathecal Infusion) for Severe Chronic Pain

Prialt is Approved for Use Only in The Medtronic SynchroMed® EL, SynchroMed® II Infusion System and Simms Deltec Cadd Micro(R) External Microinfusion Device and Catheter

NEW YORK, NY -- December 29, 2004 -- This is a MultiVu special report.

There is a new alternative for patients who suffer from severe chronic pain who require intrathecal therapy that cannot be relieved by morphine and other potent pain drugs. The FDA just approved a new analgesic called Prialt, or ziconotide intrathecal infusion. Research suggests that Prialt works by targeting and blocking calcium channels on nerves that ordinarily transmit pain signals. Prialt is administered through an appropriate implanted programmable pump that releases the drug into the fluid surrounding the spinal cord. In clinical trials, it helped alleviate pain in most patients over the long term. Dr. Michael Leong, of Stanford University and the Bay Area Pain Center, explains:

"Prialt, the man-made equivalent of a conopeptide found in the venom of the Conus magus snail, has been shown in recent clinical studies to be effective in reducing pain for patients that had failed all other therapies. More impressively for me, many of these patients decreased the amount of narcotic that they took for their chronic pain."

Severe chronic pain lasts longer than six months and has multiple causes, including failed back surgery, injury, accident, cancer, AIDS, and other nervous system disorders. For more information on severe chronic pain or Prialt, consult your physician or visit http://www.prialt.com.

Fair Balance:

Prialt has been evaluated as an IT infusion in more that 1,200 patients participating in chronic pain trials. The longest treatment duration to date is more than seven years. This combined number of patients represents the largest IT analgesic safety database ever compiled for any IT treatment, including 16 studies that were controlled and open-label studies.

Severe psychiatric symptoms and neurological impairment may occur during treatment with Prialt. Patients with a pre-existing history of psychosis should not be treated with Prialt. All patients should be monitored frequently for evidence of cognitive impairment, hallucinations, or changes in mood or consciousness. Prialt therapy can be interrupted or discontinued abruptly without evidence of withdrawal effects in the event of serious neurological or psychiatric signs or symptoms.

The most frequently reported adverse events associated with the drug in clinical trials were asthenia, nausea, vomiting, abnormal gait, ataxia, confusion, dizziness, memory impairment, nystagmus, abnormal vision, and urinary retention. It is recommended that Prialt be administered intrathecally (IT) by or under the direction of a physician experienced in the technique of IT administration and who is familiar with the drug and device labeling. Prialt is not a substitute for opioids. If opiate withdrawal is required, patients must be withdrawn slowly from opiates when initiating therapy with Prialt.

http://www.docguide.com/news/content.nsf/news/8525697700573E1885256F79005C690C

Bone replacement the coral way

Introducing Coragraf, USM's latest version of bone substitutes

For patients needing bone replacements who shudder at the thought of using bovine or porcine substitutes in their bodies, there is soon to be an alternative that is natural, disease-free, and developed by USM's very own scientists: artificial bones made from sea corals.

Named "Coragraf", the fruit of the labours of Dr Suzina Sheikh Ab. Hamid of the School of Medical Sciences, Assoc Prof Dr Abdul Rani Samsudin, Dean of the School of Dental Science and their team won a gold medal at the Invention and Innovation Contest (I-TEX) 2002 in Kuala Lumpur held from March 29-31 this year. They also won another gold medal at the 30th International Exhibition of Inventions in Geneva in May 2002.

Research on Coragraf started three years ago at the National Tissue Bank with the aim of developing a biocompatible and economical substitute to replace bones ravaged by disease or injury. Based in the USM health campus, the bank was the first of its kind in the country and was built in 1 to facilitate tissue replacement surgeries which were still at an infancy stage.

Previously, patients with congenital abnormalities, cancer or injuries due to accidents had to use allografts or bovine xenografts as bone substitutes, said Dr Rani, the bank's coordinator, who is both a maxillofacial surgeon and material science researcher.

RANI... *"Results are encouraging."*

"When we first started, we processed human bones from donors through our network of collection centres throughout the country. We were the pioneers in tissue donation, as this was way before a formal organ and tissue donation programme was formed in the country," he said.

These bones were processed by the bank and radiated at the Malaysian Institute of Nuclear Technology before being used in orthopaedic, neuro, maxillofacial and dental surgeries.

However, as the need far exceeded the supply, the bank had to look for other sources of artificial bones. Dr Rani then focused his research on bovine bones as a possible substitute in a study that lasted seven years and won him a national gold medal in 2001.

"We took the femur from one-year old calves, processed them and tested them in the laboratory, tissue culture and animal experiments. Since then, we've done bone replacement surgery on more than 1,000 patients as a result of that research, the bulk of which are dental patients," he said.

Yet it was not good enough. The popularity of human bones was decreasing, as some were found to be contaminated with Hepatitis B and the HIV virus. Patients were also wary of accepting bovine bones, as some carried an active protein causing the Cruetzfeld Jacobs Disease. Commonly known as the "mad cow disease", it degenerates the central nervous system, resulting in dementia at a very young age.

To further complicate matters, certain cultures may hesitate to use bovine or porcine bones available in the market as implants in human bodies.

"There are many cultural and religious issues involved. Bones of porcine origin, for example, may not be acceptable to certain Muslims, even though it's permissible religiously as it is for medical purposes."

"Similarly, a Hindu may object to using bovine bones in his body," he said.

This prompted the bank to look into developing synthetic bones that are free from diseases and more economical than the ones already on the market, which cost around RM1,000 to RM3,000 per gram.

Through studying the structure of the corals from the market and identifying the suitable coral species with the help of marine biologists, the team of researchers worked backwards to identify the processes used to make the bones.

"Then based on our own experience in processing bovine and human bones, we devised a method to make the corals biocompatible to the human body," said Dr Rani.

CORAL RELIEF... The coral before undergoing processing at the National Tissue Bank.

After testing the corals in the laboratory and tissue culture to ensure that they are not cytotoxic, the team conducted tests on animals, where lesions on rats and rabbits were created and the corals grafted in. The effects of the corals on the liver, kidneys and spleen were also monitored to ensure that there were no side effects.

Having done that, the team progressed to the first phase of human testing where 18 dental patients underwent coral grafting when they had their tooth extracted. The results were encouraging, as the corals were found to stop bleeding, reduce swelling and promote healing of the wounded area. The research team is now applying for ethical approval from the university's stringent human ethics committee to conduct the second phase of human research, which will be a multi-centre study.

As sea corals are a highly regulated material, the permit issued by the Fisheries Department only allows Dr Rani and his team to harvest dead corals already detached from the reef at three islands on the east coast. They are only permitted to go for three days per session, three times a year, and are limited to 5kg of corals during each visit.

However, environmental lovers need not worry, as the team has the backing of experts at the Borneo Marine Science Institute, the biggest marine research institute in the country, which verified that that the amount of corals needed to make bones has negligible effects on marine life.

Besides doing research on corals, Dr Rani is also working with Assoc Prof Razali Othman from the School of Material and Mineral Resources Engineering on using hydroxy apatit (calcium phosphate) to make synthetic bones derived from che-mical synthesis. They are currently developing the product and are awaiting approval from the ethical committee for phase one of human research.

http://www.usm.my/r&d/frontiers/f2/3.html

NSTA 2005 Biotechnology Resources

www.nmsfocean.org/chow2003/powerpoint/pomponi.pdf
"The Oceans and Human Health: Drugs from the Deep" Dr. Shirley Pomponi's powerpoint presentation.

www.flseagrant.org/program_areas/biotechnology/biotech_cr.htm
"Marine Biotechnology Research at Florida Sea Grant"

http://oceanexplorer.noaa.gov/explorations/03bio
Detailed mission logs

http://scrippsnews.ucsd.edu/article_detail.cfm?article_num=661
(December 9, 2004) "Cloned Gene from Sea Animal May Prove Key in Cancer Drug Development" article and video clips of Dr. Haygood describing Bryozoan.

http://www.nature.com/news/2004/040621/pf/040621-6_pf.html
Cone snail article

http://www.oar.noaa.gov/spotlite/archive/spot_delaware.html
"The Horseshoe Crab -- Putting Science to Work to Help "Man's Best Friend" -- University of Delaware Sea Grant College Program"

http://horseshoecrab.org/med/med.html
Medical uses of Horseshoe crabs

http://www.reefcheck.org/articles/june_03/marine_pharmacology.pdf
Article about *pseudopterosins* – Estee Lauder cosmetic products

http://chapmanlab.lsu.edu/digitalalgae/GulfAlgae/MMSBiotech.html
Algae article

http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=427802
Mussel article

http://www.ocean.udel.edu/horseshoecrab/Research/chitin.html
Chitin article

http://www.msi.ucsb.edu/msilinks/mbc/mbctexts/mbc.htm
Sea urchin article

http://www.usm.my/r&d/frontiers/f2/3.html
Coral article

http://www.cancerchoices.com/squalamine.htm
Squalamine article