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Medicines from the Deep Sea: Exploration of the Gulf of Mexico

The Benthic Drugstore

Focus
Pharmacologically-active chemicals derived from marine invertebrates

Grade Level
9-12 (Life Science)

Focus Question
What pharmacologically-active chemicals are obtained from marine invertebrates, and how do these chemicals act to fight disease in humans?

Learning Objectives
Students will be able to identify at least three pharmacologically-active chemicals derived from marine invertebrates.

Students will be able to describe the disease-fighting action of at least three pharmacologically-active chemicals derived from marine invertebrates.

Students will be able to infer why sessile marine invertebrates appear to be promising sources of new drugs.

Materials
❒ Marker board, blackboard, or overhead projector with transparencies for group discussions

Audio/Visual Materials
None

Teaching Time
One or two 45-minute class periods, plus time for student research

Seating Arrangement
Groups of 4-6 students

Maximum Number of Students
30

Key Words
Cardiovascular disease
Cancer
Arthritis
Natural products
Sponge
Tunicate
Ascidian
Bryozoan
Octocorals
Ecteinascidin
Topsentin
Lasonolide
Discodermalide
Bryostatin
Pseudopterosins
ω-conotoxin MVIIA

Background
Despite the many advances of modern medicine, disease is still the leading cause of death in the United States. Cardiovascular disease and cancer together account for more than 1.5 million deaths annually (40% and 25% of all deaths, respectively). In addition, one in six Americans have some form of arthritis, and hospitalized patients are increasingly threatened by infections that are resistant to conventional antibiotics. The cost of these diseases is staggering: $285 billion per year for cardiovas-

cular disease; $107 billion per year for cancer; $65 billion per year for arthritis. Death rates, costs of treatment and lost productivity, and emergence of drug-resistant diseases all point to the need for new and more effective treatments.

Most drugs in use today come from nature. Aspirin, for example, was first isolated from the willow tree. Morphine is extracted from the opium poppy. Penicillin was discovered from common bread mold. To date, almost all of the drugs derived from natural sources come from terrestrial organisms. But recently, systematic searches for new drugs have shown that marine invertebrates produce more antibiotic, anti-cancer, and anti-inflammatory substances than any group of terrestrial organisms. Particularly promising invertebrate groups include sponges, tunicates, ascidians, bryozoans, octocorals, and some molluscs, annelids, and echinoderms.

The goal of the 2003 Medicines from the Deep Sea Expedition is to discover new resources with pharmaceutical potential in the Gulf of Mexico. To achieve this goal, the expedition will:

- collect selected benthic invertebrates from deep-water bottom communities in the Gulf of Mexico (sponges, octocorals, molluscs, annelids, echinoderms, tunicates), identify these organisms, and obtain samples of DNA and RNA from the collected organisms;
- isolate and culture microorganisms that live in association with deep-sea marine invertebrates;
- prepare extracts of benthic invertebrates and associated microorganisms, and test these extracts to identify those that may be useful in treatment of cancer, cardiovascular disease, infections, inflammation, and disorders of the central nervous system;
- isolate chemicals from extracts that show pharmacological potential and determine the structure of these chemicals;
- further study the pharmacological properties of active compounds; and
- develop methods for the sustainable use of biomedically important marine resources.

The last objective is particularly important, since many potentially useful drugs are present in very small quantities in the animals that produce these drugs. This makes it impossible to obtain useful amounts of the drugs simply by harvesting large numbers of animals from the sea. Some alternatives are chemical synthesis of specific compounds, aquaculture to produce large numbers of productive species, or culture of the cells that produce the drugs.

This activity is designed to familiarize students with some of the promising biologically-active chemicals that have been isolated from marine sources and with the organisms that produce these chemicals.

Learning Procedure

1. Review the importance of finding new drugs for the treatment of cardiovascular disease, cancer, inflammatory diseases, and infections. Describe the potential of marine communities as sources for these drugs, and introduce the objectives of the 2003 Medicines from the Deep Sea Expedition.

2. Tell students that their assignment is to prepare a written report on a substance that has been isolated from a marine benthic invertebrate and that has potential for treating human diseases. Reports should include:
   - information about the chemistry of the substance;
   - what organisms produce the substance;
   - basic life history information about these organisms (where they live, what they eat)
   - possible functions of the substance in these organisms; and
   - how the substance acts in the treatment of human disease.

Assign each student or student group one or more of the following biologically-active chemicals: You may want to direct students to "Marine

Pharmacology" and/or CancerQuest (see Resources).
- Ecteinascidin
- Topsentin
- Lasonolide
- Discodermalide
- Bryostatin
- Pseudopterosins
- ω-conotoxin MVIIA

3. Have students orally summarize their reports, and lead a discussion of the results. Reports should include the following points:

Ecteinascidin – Extracted from tunicates; being tested in humans for treatment of breast and ovarian cancers and other solid tumors; acts by blocking transcription of DNA

Topsentin – Extracted from the sponges T*opsentia genitrix*, *Hexadella sp.*, and *Spongosorites* sp.; anti-inflammatory agent; mode of action not certain

Lasonolide – Extracted from the sponge *Forcepia* sp.; anti-tumor agent; acts by binding with DNA

Discodermalide – Extracted from deep-sea sponges belonging to the genus *Discodermia;* anti-tumor agent; acts by intefering with microtubule networks (you may want to review the function of microtubules here)

Bryostatin – Extracted from the bryozoan *Bugula neritina;* potential treatment for leukemia and melanoma; acts as a differentiating agent, forcing cancer cells to mature and thus halting uncontrolled cell division

Pseudopterosins – Extracted from the octocoral (sea whip) *Pseudopterogorgia elisabethae;* anti-inflammatory and analgesic agents that reduce swelling and skin irritation and accelerate wound healing; acts as an inhibitor of phospholipase A, which is a key enzyme in inflammatory reactions

ω–conotoxin MVIIA – Extracted from the cone snail, *Conus magnus;* potent pain-killer; acts by interfering with calcium ion flux, thereby reducing the release of neurotransmitters

Students should recognize that all of these species are sessile. Tell students that to date, this has been true of most marine invertebrates that produce pharmacologically active substances. Several reasons have been suggested to explain why sessile marine animals are particularly productive of potent chemicals. One possibility is that they use these chemicals to repel predators, since they are basically "sitting ducks." Since many of these species are filter feeders, and consequently are exposed to all sorts of parasites and pathogens in the water, they may use powerful chemicals to repel parasites or as antibiotics against disease-causing organisms. Competition for space may explain why some of these invertebrates produce anti-cancer agents: if two species are competing for the same piece of bottom space, it would be helpful to produce a substance that would attack rapidly dividing cells of the competing organism. Since cancer cells often divide more rapidly than normal cells, the same substance might have anti-cancer properties.

The BRIDGE Connection

www.vims.edu/bridge/ – Click on "Ocean Science" in the navigation menu to the left, then "Chemistry" for resources on drugs from the sea. Click on "Ecology" then deep sea for resources on deep-sea communities. Click on "Human Activities" then "Technology" then "Biotechnology" for resources on biotechnology.

The "Me" Connection

Have students write a short essay about deep-sea organisms might benefit them personally in ways other than as sources of potentially important drugs.

Connections to Other Subjects

English/Language Arts; Chemistry

Evaluation

Written and oral reports provide opportunities for evaluation.

Extensions

Log on to http://oceanexplorer.noaa.gov to keep up to date with the latest discoveries of the 2003 Medicines from the Deep Sea Expedition.

Visit http://www.woodrow.org/teachers/bi/1993/ for more activities related to biotechnology from the 1993 Woodrow Wilson Biology Institute.

Resources

http://oceanica.cofc.edu/activities.htm – Project Oceanica website, with a variety of resources on ocean exploration topics

http://www.science.fau.edu/drugs.htm – An overview article on drugs from the sea

Faulkner, D. J. 2000. Marine pharmacology. Antonie van Leeuwenhoek 77:135-145. Available online at http://www.reefcheck.org/headlines/june/pdf/marine_pharmacology.pdf.

www.nci.nih.gov – Website of the National Cancer Institute

http://www.woodrow.org/teachers/bi/1993/ – Background and activities from the 1993 Woodrow Wilson Biology Institute on biotechnology

http://www.cancerquest.org – CancerQuest website; includes an introduction to cell biology; structure and action of anti-cancer drugs

National Science Education Standards

Content Standard A: Science as Inquiry

- Abilities necessary to do scientific inquiry
- Understandings about scientific inquiry

Content Standard B: Physical Science

- Structure and properties of matter
- Chemical reactions

Content Standard C: Life Science

- The cell
- Interdependence of organisms
- Behavior of organisms

Content Standard F: Science in Personal and Social Perspectives

- Personal and community health
- Natural resources
- Science and technology in local, national, and global challenges

For More Information

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