



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

# The Electric Sieve

### FOCUS

Separation of complex mixtures

### GRADE LEVEL

9-12 (Chemistry)

### FOCUS QUESTION

How can complex mixtures, particularly mixtures of organic substances, be conveniently separated?

### LEARNING OBJECTIVES

Students will be able to explain and carry out a simple process for separating complex mixtures.

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

### MATERIALS

- Gel casting trays (Carolina Biological Supply No. WW-21-3655)
- Electrophoresis chambers and power supplies (see "Learning Procedure")
- 1% agarose gel (Carolina Biological Supply No. WW-21-7075)
- TRIS/Borate/EDTA buffer (Carolina Biological Supply No. WW-21-9025)
- Four test tubes, each containing a pure food color, plus a fifth test tube containing a mixture of food colors; one set for each student group
- Five micropipets (Carolina Biological Supply No. WW-21-1022)
- Paper towels
- Plastic sandwich bag, one for each student group
- Student instruction handout for each student (see

"Learning Procedure")

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

### AUDIO/VISUAL MATERIALS

None

### TEACHING TIME

One or two 45-minute class periods

### SEATING ARRANGEMENT

Groups of 2-3 students

### MAXIMUM NUMBER OF STUDENTS

30

### KEY WORDS

Cardiovascular disease  
Cancer  
Arthritis  
Natural products  
Electrophoresis

### BACKGROUND INFORMATION

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 cardiovascular 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 list of drugs derived from marine invertebrates includes:

**Ecteinascidin** – Extracted from tunicates; being tested in humans for treatment of breast and ovarian cancers and other solid tumors

**Topsentin** – Extracted from the sponges *Topsentia genitrix*, *Hexadella* sp., and *Spongosorites* sp.; anti-inflammatory agent

**Lasonolide** – Extracted from the sponge *Forcepia* sp.; anti-tumor agent

**Discodermalide** – Extracted from deep-sea sponges belonging to the genus *Discodermia*; anti-tumor agent

**Bryostatin** – Extracted from the bryozoan *Bugula neritina*; potential treatment for leukemia and melanoma

**Pseudopterosins** – Extracted from the octocoral (sea whip) *Pseudopteroorgia elisabethae*; anti-inflammatory and analgesic agents that reduce swelling and skin irritation and accelerate wound healing

**ω-conotoxin MVIIA** – Extracted from the cone snail, *Conus magnus*; potent pain-killer

This list reflects an interesting fact about invertebrates that produce pharmacologically-active substances: most species are sessile; they are immobile and live all or most of their lives attached to some sort of surface. Several reasons have been suggested to explain why these particular animals produce potent chemicals. One possibility is that they use these chemicals to repel predators, since they are sessile, and thus 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 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. Some techniques for producing specific drugs are based on the cells' own machinery for chemical synthesis: enzymes, guided by information contained in the cells' DNA and RNA.

This activity is designed to acquaint students with electrophoresis, one of the techniques that can be used to separate active components from crude extracts that show biological activity.

### LEARNING PROCEDURE

[NOTE: This lesson is based upon activities designed by Karen Kyker, Sandy Collins, and Theresa Knapp while participating in the 1993 Woodrow Wilson Biology Institute. These activities are used with permission from the Woodrow Wilson National Fellowship Foundation. Visit <http://woodrow.org> for information on other activities and current programs.]

1. Download the following activities:
  - "Electrophoresis Analogy" (<http://www.woodrow.org/teachers/bi/1993/electrophoresis.html>)
  - "Rainbow Electrophoresis" (<http://www.woodrow.org/teachers/bi/1993/rainbow.html>)
  - "Desktop Electrophoresis Lab - Moving Molecules" <http://www.woodrow.org/teachers/bi/1993/moving.html>
2. Prepare electrophoresis gels, TRIS/Borate/EDTA buffer, and student instruction sheets (from the downloaded activities) prior to the lab. If you want to use the (lower cost) "Desktop Electrophoresis" apparatus, prepare the chambers and power supplies as well, unless you plan to have students do this.
3. Discuss 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 briefly discuss some potentially useful drugs that have been discovered from these communities. Ask students to list some reasons that these kinds of drugs might be found primarily among sessile invertebrates. Briefly introduce the objectives of the 2003 Medicines from the Deep Sea Expedition. Highlight the initial steps in the search for new drugs, and tell students that they will be learning to use one of the techniques for separating individual components from complex mixtures. Introduce the technique of electrophoresis using the "Electrophoresis Analogy."
4. Have students complete the "Rainbow Electrophoresis" lab activity as directed in the student instructions. Each group should prepare written answers to the questions included in the activity.
5. Have each group make a brief presentation of their results. Lead a discussion of how this lab activity relates to the process of actually searching for new drugs (this is a good opportunity to

There are two options for obtaining the equipment needed for this activity. The first is to buy electrophoresis chambers and power supplies from a laboratory supply company (cost approximately \$400 and up). The second is to build your own chambers and power supplies as directed in the "Desktop Electrophoresis Lab" activity (cost approximately \$20 per system).

interact with the scientists on the Medicines from the Deep Sea Expedition).

Discuss the process of developing a useful drug from a marine organism. The first step, of course, is to locate a promising candidate. This involves “prospecting” among many different species, though past experience suggests some groups (sessile invertebrates) that may be particularly promising. Extracts of each species are prepared, usually by grinding tissue from the organisms in organic solvents. Next, the extracts are tested for pharmacological activity through a series of bioassays (for example, finding out whether an extract can kill leukemia cells or reduce inflammation). When an extract is found to have positive biological activity, the active substance in the extract is isolated and identified. If the isolated chemical turns out to be new, the next step is to test the chemical in animal models (for example, mice with tumors). If animal testing is successful, the chemical may be approved for evaluation in humans. If the chemical is effective in humans without toxic side effects, it may be approved as a new drug. The entire process can take a lot of time and money; a new anti-cancer drug may require 10 – 20 years and an average of \$40,000,000 to develop to the point of commercialization.

### THE BRIDGE CONNECTION

[www.vims.edu/bridge/](http://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 how undiscovered organisms might benefit them personally in ways other than as sources of potentially important drugs.

### CONNECTIONS TO OTHER SUBJECTS

English/Language Arts; Life Science

### EVALUATION

Written reports in Step 4 provide an opportunity for assessment.

### 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.

Have students perform additional separation of other complex mixtures. Biological supply companies have a variety of materials and kits suitable for applying electrophoresis to DNA study, forensic investigations, etc.

### RESOURCES

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

[http://www.reefcheck.org/headlines/june/pdf/marine\\_pharmacology.pdf](http://www.reefcheck.org/headlines/june/pdf/marine_pharmacology.pdf) – Marine pharmacology

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](http://www.reefcheck.org/headlines/june/pdf/marine_pharmacology.pdf).

[www.nci.nih.gov](http://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://spikesworld.spike-jamie.com/science/index.html> — Website with lots of background and activities on multiple science topics

### 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

#### Content Standard E: Science and Technology

- Understandings about science and technology

#### 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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<http://oceanexplorer.noaa.gov>