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Aqua Farm News

1995

Aqua Farm News Volume 13(05)

September - October 1995

Aquaculture Department, Southeast Asian Fisheries Development Center

<http://hdl.handle.net/10862/2487>

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AQUA FARM NEWS



ISSN 0116-6573

A publication of SEAFDEC Aquaculture Department, Iloilo, Philippines

Vol. XIII No. 5

September-October 1995

Drugs from the Sea

Pharmaceutical products or drugs from the sea are not aquaculture concerns. But when likely sources are already farmed like the seaweeds or have aquaculture potential like the sponges, then it would be worthwhile to take a closer look at this discipline.

SEAFDEC/AQD farming technology

SEAFDEC Aquaculture Department does not screen for biological activity of compounds extracted from marine organisms but it does conduct studies on farming some of these organisms. Notable is the farming of the seaweeds *Gracilaria* and *Kappaphycus*. In addition, SEAFDEC/AQD's vast library collection includes the latest technologies in aquaculture. SEAFDEC/AQD also collaborates with the University of the Philippines which conducts research on bioactive compounds, among others.



The discussion in this issue basically follows the process on how drugs from marine sources are isolated and produced. Exception is made, however, for processes totally biomedical in nature. Folk medicine in the Philippines is highlighted. Ditto with research at SEAFDEC/AQD and the University of the Philippines - Visayas. An overview of the Philippines' Bureau of Food and Drugs is included.

The Chemical Prospectors

With little new ground gained in the war against cancer, no cure in sight for AIDS, and the looming threat of resistance to current antibiotics, modern researchers have become as intrigued by new natural pharmaceuticals as 15th-century explorers were by spices. Collectors search for specimens around the world, in remote jungles, coral reefs, marshes, and the depths of the ocean. And although it costs twice as much to get a specimen from the sea as it does to collect a terrestrial item, the effort is proving worthwhile. Today most natural compounds that show promise as anti-cancer drugs come from the sea. These include six compounds that have reached clinical or late-preclinical trials in the United States and Canada.

Marine chemists say they have only just begun to tap the chemical diversity of the sea. "Man has been interacting with plants on land for some 3000 years," says chemist William Fenical of the Scripps Institution of Oceanography. "In the ocean there are an incredible number of organisms - and we don't know their potential."

And it is not just the U.S. researchers who are looking to the oceans. The Japanese government is starting to emphasize marine natural products, and Japan has become the world leader in the use of submersibles for collecting deep-water organisms. So far, Japanese researchers haven't found anything that has reached the clinical trial stage. Also, they don't have a massive screening effort like the US National Cancer Institute (NCI). But Japanese scientists have isolated a number of potential anti-cancer and antibiotic compounds especially from deep-

sea bacteria, and used crystallography or other techniques to determine their chemical structures which are often strange and unique.

Toxic defense

One reason sea creatures are particularly promising sources of anti-cancer compounds, speculates NCI chemist David Newman, is that natural selection has forced them to develop elaborate chemical arsenals. The sea is full of

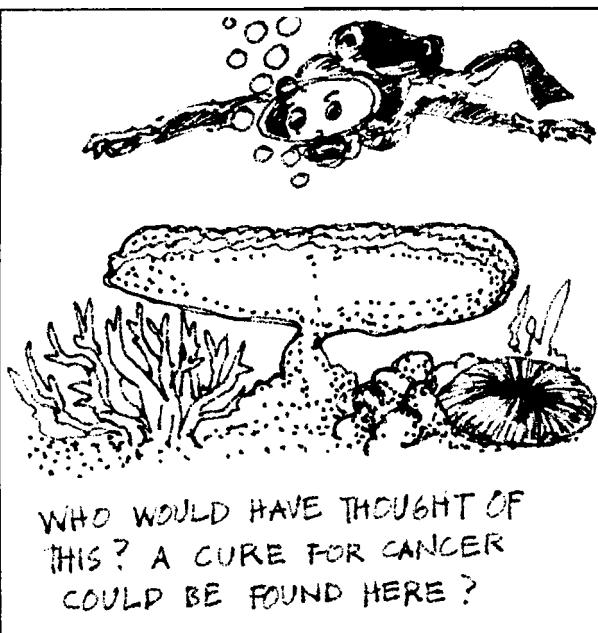
sitting targets: soft-bodied, stationary, brightly colored creatures that seem to say "eat me", he says. To avoid that fate, those creatures rely on powerful toxins. And toxicity is the reason cancer drugs work - the goal is to poison tumor cells more than healthy cells.

Collectors look for soft bodies and other signs of helplessness. Most of the samples come from the warm tropics, and although it's likely that those regions hold more biodiversity,

a simpler explanation is that divers like the tropics, as Newman says. "I've gone diving off England. And it's bloody cold..."

Research has been given a boost by the development of screening techniques based on the tools of molecular biology. These screens generally look for a compound's effects on a specific chemical "target" -- usually an enzyme responsible for the growth of cancer cells. The speed of the molecular screens has revolutionized the search for drugs from natural products, says Crews. "You can screen thousands of things each day now."

Using this new technology, Crews, in collaboration with researchers from Syntex in California, has identified two possible cancer-fighting



compounds from sponges. One is a class of compounds called **bastadins** that interfere with the growth of leukemic cells and ovarian tumors; the other is a compound called **jasplakinolide**, which disrupts cell division in cultured renal and prostate cancer cells. Jasplakinolide has a serious drawback as a potential therapeutic agent. It is so toxic that it killed all the lab animals exposed to it. The hope, however, is that chemists will be able to alter the compound's structure to produce a milder derivative that retains enough toxicity to deal with tumor cells.

Researchers at Smith Kline Beecham are also using fast assays to plow through thousands of organisms they pluck from coral reefs, estuaries, marine lakes, and even wrecked ships, says Brad Carte, a marine products chemist. "We look for anti-cancer drugs, anti-inflammatory, antivirals, anything you can think of." They test extracts to see if they inhibit a target enzyme called a topoisomerase, enzymes that, by changing the topology of DNA, are important in the proliferation of cancer cells. They've used this to identify promising small molecules from several sponges from the Philippines and Japan, one of which has shrunk tumors in mice.

The company has also screened for chemicals that bind to an enzyme called protein kinase, which is essential for cell division and signal transduction -- the transfer of information from outside chemicals, such as growth factors and hormones, into cells. A drug acting against protein kinase might inhibit cancer growth or inflammation. Paul Scheuer of the University of Hawaii and his colleagues have identified protein kinase inhibitors from a sponge and a tunicate. And while NCI has found just one compound that has any effect on HIV, University of Chicago researchers have seen sponge extracts that inhibit HIV protease, an enzyme necessary for viral replication.

Microbial prospecting

While most researchers have been testing extracts from large organisms, others, including microbiologist Deborah Steinberg of American

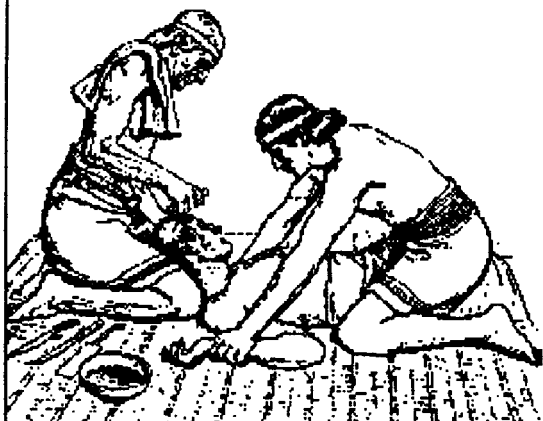
“If a useful drug turns up, researchers could quickly face a problem: demand may outstrip supply. Researchers try to prevent that by developing techniques for farming marine organisms.”

Cyanamid, have been thinking small. They are scouring the seas for microorganisms with potentially useful properties. She and her colleagues collect microbes from around the world and use a variety of molecular screens and tested them for signs of antibiotic, anti-cancer, or anti-viral properties, as well as potential for cardiovascular and central nervous system drugs. They test thousands per day right on the collection ship and have already found a number of leads. One is **bioxalomycin** -- a compound isolated from shoreline bacteria that shows antibacterial properties.

Scripps's Fenical is now working with Bristol-Myers Squibb to screen marine microbes for both anti-cancer and anti-inflammatory agents. Though his team searches water and sand, he's actually found the most interesting samples on the bodies of other organisms. "We look on the surfaces of plants and animals," he says, "in the tissues of fish and the digestive tracts of shrimp."

Indeed, some of the toxins associated with macroscopic animals come from microbes that live in or on their bodies. Take **tetrodotoxin**, a deadly substance that concentrates in the puffer fish -- and occasionally kills daredevil gourmets who indulge in this high-risk delicacy. Japanese biochemists Takeshi Yasumoto of Tohoko Uni-





Ouch! That hurts!

Quite a long time ago, surgeons remove a section of bone from the skull to relieve pressure on the brain. First, the patient's head was shaved and the skin slit and drawn back, exposing the bone. Then a small surgical saw was used to remove the section, which was replaced when the drainage was completed. The hole remaining in the skull indicates that the patient died.

Surgeries in the 21st century are much less painful with the discovery of anaesthesia. Preventive drugs have also been discovered from both land-based and aquatic organisms. More bioactive compounds especially from aquatic organisms are being studied by scientists.

Reference: *Great People of the Bible and How They Lived*. 1974. The Reader's Digest Association, Inc. New York. p. 202.

versity and Michlo Murata of the University of Tokyo recently discovered that tetrodotoxin comes from a type of unicellular marine bacteria living in the fish's internal organs.

Fenical has found that many marine creatures and their eggs are covered with bacteria that protect their hosts from disease: "If you put organisms in polluted seawater and destroy the surface bacteria, the animals die because they get infected with pathogens." That finding, he says, argues for seeking new antibiotics in such protective microbes. Already, he has interesting leads, including a powerful anti-fungal compound, called **istatin**, isolated from bacteria that protect shrimp eggs, and two possible antibiotics, **salinamide A and B**, in bacteria living on the body of a jellyfish found in Florida.

Supply and demand

If a useful drug does turn up, researchers could quickly face a problem: demand may outstrip supply. Crews and other researchers are trying to prevent that by developing techniques for farming marine organisms. It can be a challenging task, however, for some creatures -- sponges, for example -- are notoriously difficult to cultivate, says Crews. One group, headed by marine chemists Murray Munroe and John Blunt

at the University of Canterbury in New Zealand, has managed to start the first sponge farm, growing the sponge that produces halochondrin -- one of the six marine-based compounds that are moving toward clinical trials.

Microbes should be easier to grow, but even here, the strangeness of the marine world presents a challenge. "You have to reinvent microbiology," says Fenical. Terrestrial bacteria are often grown in protein compounds or glucose. But "there's no glucose in the sea." So to grow marine microbes, he says, "we've developed about 25 media based on all kinds of concoctions - fish meals and powders, special oils, and crab shells. ... You have to think about what's out there."

Chemical prospecting among marine organisms is still in its early stages. But with several compounds showing promise in the lab and a handful moving toward clinical trials, researchers like Fenical are confident that it is just a matter of time before they hit pay dirt. And, when that happens, the big drug companies will follow. "Within the next 5 years companies will look into the ocean as they've never done before," he says.

Excerpted from *Science* Vol. 266. November 25, 1994.

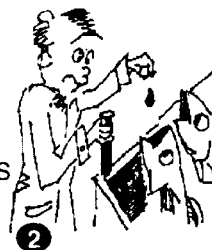
HOW DRUGS FROM MARINE SOURCES ARE ISOLATED AND PRODUCED



PRELIMINARY ISOLATION
Drug suggested by analogy or general screening program

1

SCREENING AND DISCOVERIES
Unique or potentially useful biological activity is found

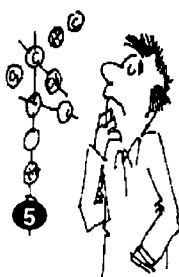


2



SOURCE MATERIALS
Obtain enough material to isolate and characterize active compound(s)

3



CHARACTERIZATION AND SYNTHESIS

5

EFFECTIVE CHEMOTHERAPY
Test for efficiency in treatment of animals



4

MASS SCALE SYNTHESIS



6



PHARMACOLOGICAL STUDIES
Testing for drug activity and safety

7



GOVERNMENTAL APPROVAL

- Disclosure of complete drug source and manufacturing information
- Preclinical results disclosed
- Future research plans and other supporting data

8



CLINICAL EVALUATION

- Testing with human volunteers to determine metabolism, absorption and elimination, side effects, safe dose range, preferred method of administration. Obtain therapeutic index (value versus hazards).
- Initial diagnosis test
- Outside controlled tests

MASS PRODUCTION
Economic, governmental, technical limitations apply



10



MARKETING PROCEDURES
Economic, governmental, technical limitations apply

11

Illustrated by I. Tendencia. Reference: MT Doig III, DF Martin, GM Padilla. 1973. *Marine bioactive agents: chemical and cellular correlates*, p. 6. In: DF Martin and GM Padilla (eds). *Marine Pharmacognosy Action of Marine Toxins at the Cellular Level*. Academic Press, New York. 317 p.



STEP 1
PRELIMINARY
ISOLATION
Drug suggested by
analogy or
general screening
program



Folk medicine and horticulture


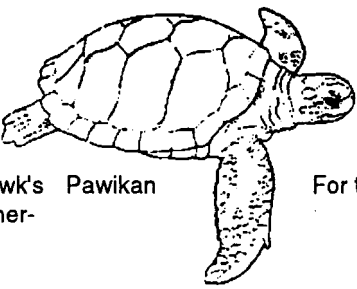
Marine organisms are used in folk medicine by coastal people of northern Mindanao and the Visayan islands of Bohol, Cebu and Negros in central Philippines. Of particular interest are concoctions used to treat malaria, bleeding, fertility problems, and worm infection (table below lists those related to aquaculture). There could be truly effective drugs from marine organisms.

Sea urchins contain bioactive substances. Mangroves contain tannins, phenolic compounds that exhibit antimicrobial activity. Seaweeds contain phenols and terpenoidal compounds.

In horticulture and agriculture, Filipino coastal dwellers have used brown seaweeds as soil ameliorant and growth enhancer. Studies point out that seaweed extracts contain plant growth-promoting substances. These are now exploited commercially. Other studies indicate the possible use of seaweeds directly as fertilizer. In northern Cebu, starfish is used as coconut fertilizer; it reportedly induces blooming and produces healthier trees. Studies has also been made on the use of sea urchins and seaweeds as vermifuge.

Common name	Local name	Treatment or use
Green seaweed	Lato, ar-arucip	For treatment of rheumatism. Seaweed is boiled and its soup drunk. For treating or preventing goiter. Seaweed is eaten raw or prepared as salad.
Green seaweed	Lukay-lukay	For treatment or prevention of goiter or <i>bugon</i> and colds. Seaweed is eaten raw or prepared as salad.
Brown seaweed	Boto-boto, lusay-lusay, aragan	For treatment of goiter and other glandular troubles. Seaweed is boiled, the soup drunk. Young shoots may be added to <i>paksiw</i> dishes (recipes consisting of fish cooked in vinegar, ginger, garlic and salt).
Brown seaweed	Samo, aragan	Dried seaweeds are burned with or without small pieces of rubber to drive away insects particularly those that infect rice fields. Dried seaweeds may also be hung on trees -- like the <i>upo</i> or <i>Lagenaria siceraria</i> and the <i>langka</i> or jackfruit <i>Artocarpus integrifolia</i> -- that are infested with worms. Seaweeds are believed to drive away the insects. These may also be mixed with soil as conditioner or with rice bran as hog feed.
Red seaweed	Gulaman	For treatment of stomach disorders; also used as laxative. Decoction is prepared and drunk.
Red seaweed	Guso, tamsao, cottonii	Decoction is used as foliar spray to enhance flowering and crop growth.

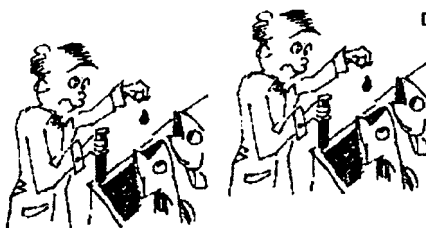


Common name	Local name	Treatment or use
		
Giant clam	Taklobo	For malaria; the meat is eaten raw or boiled.
Black sea urchin	Tuyom, salunggo, tayong-tayong	As pig vermifuge. The fluid inside the urchin test and the aristotle's lantern is used.
Sea urchin		As purgative for man and pigs. Sea urchin is chopped or pounded, boiled, and the soup is drunk.
Sea cucumber	Bahay-bahay, balat	For errant husbands. The sea cucumber is dried, then, placed in the trousers (inside pockets or seams) of the husband. Believed to cause impotence.
Grouper	Lapu-lapu, lig-lig	For faster healing of wounds of women who gave birth. Blood from the tail of the fish is extracted and drunk.
Rabbitfish	Danggit, samaral	For treatment of wound caused by fish spines. Fish liver is applied on the wound.
		
Green turtle, hawk's bill turtle, leather-back turtle	Pawikan	For treatment of asthma. The flesh is cooked <i>adobo</i> -style (with vinegar, soy sauce, garlic, laurel leaves, pepper corn and salt) and eaten. The flesh may be broiled slightly burned, placed in water, and the soup drunk. As aphrodisiac. The turtle eggs are believed to stimulate sexual drive.
Crocodile	Buaya	For sexual potency. The sexual organ is cooked and eaten.
Mangrove	Pagatpat, miyapi	For stomach aches. The bark is boiled and the extract drunk or used to wash wounds. Tannins from boiled mangrove is considered an omnipotent medicine. Used as antiseptic.
Seawater	Tubig sa baybay o dagat	Used for faster healing of wounds. During summer in eastern Visayas, newly circumcised boys ages 7 -10 bathe in the sea to heal their wounds faster. For treatment of partial paralysis caused by stings of poisonous sea urchins or fishes. Hot seawater is applied on the wound, or the area is immersed in hot seawater.
Hot mud from ponds and mangrove areas		Used for faster healing of wounds and sores. Hot mud is applied on wounds and sores.
White sand from the sea		For treatment of wounds caused by thorns of marine animals. Sand is chewed and applied externally to the wound.
Oysters	Sisi, talaba	Shells are ground and applied to plants as fertilizers or soil ameliorant. Ground shells are mixed with grain for use as feeds for fowls.
Washing of fish (blood and scales)		Applied to ornamental plants to enhance growth and blooming.

References: (1) **Research Gems**. UP Diliman, 1991. UP, Diliman, Quezon City. (2) PM Aliño, GJB Cajipe, ET Ganzon-Fortes, WRY Licuanan, NE Montaño, and LM Tupas. *Some traditional medicinal and horticultural uses of marine organisms*. SICEN Leaflet 1.

Toxicity test: sponge toxin on tilapia fry

STEP 2
SCREENING
AND
DISCOVERIES
Unique or
potentially
useful
biological
activity
is found



The toxicity of extracts from five species of marine sponges was tested on tilapia *Oreochromis niloticus* fry. Two kilograms of each sponge were collected by skin diving off Sebaste, Guimaras in west central Philippines. The species were chosen arbitrarily, harvesting whatever was plentiful at the time of diving. The depth from where sponges are collected ranged 3-7 meters. Sponges were collected at different habitats — reef top, sandy shore, deep sandy substratum, and deep rock.

In the laboratory, sponge toxins were extracted using water or methanol. Each sponge sample was minced, homogenized with water, sieved, then centrifuged. The resulting liquid suspension was deep frozen then freeze-dried until used. This was the water extract. The remaining solid (after centrifugation) was oven-dried, milled, mixed in methanol, shaken and agitated, then allowed to settle. The resulting liquid was centrifuged then concentrated in a rotary evaporator. The concentrate was oven-dried until it was reduced to paste or gum. This is the methanol extract.

The toxin extracts (water and methanol) were tested on tilapia fry. For the range-finding tests, toxin concentrations used were 0.01, 0.1, 1.0, 10, 100 and 200 ppm. For the definitive tests, the range was from 0.06 to 512 ppm.

The test tilapia fry were about 10.9 mm and 17.6 mg. About 20 fry were placed in each 3-liter test tank. Water temperature, salinity, pH and dissolved oxygen were monitored. Fish behavior and mortality were monitored every 15 minutes during the first hour, every hour for the next five hours, and every two hours for the rest of the 98 hours. Before dying, the fish either:

- gulped air at the surface
- convulsed or swam spasmodically
- swam in circles or whirled sometimes with head on the tank bottom
- swam with the body sideways or upside down
- floated at or below the surface, sometimes upside down
- rested motionless at the bottom, upright or on its side
- did not respond when touched
- swam to the surface vertically
- crawled on its side
- changed color (to darker shade)

The concentrations of the sponge toxins and the time it took to kill 50% of the tilapia fry — termed LC₅₀ — are tabulated:

Sponge species	LC50 (ppm)	Hours
<i>Dysidea herbacea</i> (methanol extract)	2.5	36
<i>Dysidea herbacea</i> (water extract)	39.2	60
<i>Gelloides callista</i> (water extract)	95.3	24
<i>Sigmatocia symbiotica</i> (water extract)	59.5	60
<i>Spirastrella vagabunda</i> (methanol extract)	125.5	60
<i>Callyspongia exigua</i> (water extract)	398.0	36

The most potent appears to be the methanol extract of *Dysidea herbacea*; it kills with the least toxin and at the shortest time.

Reference: GT Tayo. 1989. *Toxicity of some Philippine sponges*. *Kinaalam* 2 (2): 83-86. *Kinaalam* (the local term for knowledge or wisdom) is a publication of the Graduate School, University of the Philippines in the Visayas, Miagao, Iloilo 5023, Philippines.





STEP 3
SOURCE MATERIALS
Obtain enough material
to isolate and
characterize active
compound(s)



Farming seaweeds at SEAFDEC/AQD

At the SEAFDEC Aquaculture Department in the Philippines, a few practices have been established or documented for seaweeds.

Cage culture of *Kappaphycus*

The seaweed *Kappaphycus alvarezii* var. *tambalang* can be cultivated in 3 x 3 m bamboo rafts placed inside a floating net cage stocked with sea bass (a carnivore). This type of integrated culture makes better use of marine resources, reduces the impacts of more intensive aquaculture, minimizes grazing, and maximizes production.

Individual cuttings weighing 150-200 grams are tied to a 3-m nylon line (#110) and spaced 20 cm apart. Nine lines are tied 30 cm apart to the raft. The raft is placed inside a 4 x 4 m floating net cage containing sea bass broodstock. It is kept submerged with stone sinkers 25-30 cm below the surface.

Kappaphycus is left to grow for 30 days. In culture trials conducted by SEAFDEC from January to May 1990, seaweed grew at 3-7% per day. Water temperature was about 28-30°C, salinity 33-35 ppt, and pH 8.05-8.35. Epiphytism was limited to the bamboo raft and to the unplanted monoline cord.

Production varied from 500 to 2,000 grams per line meter or a monthly production of 25 tons per hectare (fresh) or 7.5 tons (dry). This is comparable to commercial production.

Farming *Gracilaria*

Seaweed growers in Panay island (west central part of the country) use the "rice planting" method. *Gracilaria* is cultivated in brackishwater ponds or in canals. The area cultivated ranged from 0.5 to 5 hectares for ponds and 825 to 7055 m² for canals. Farmers use local stocks as seedstocks. For planting, they use thalli that

measure 15-20 cm or weigh 15-20 g. A thalli bunch is staked into the pond or canal (substrate is usually sandy-muddy). The bunches are spaced 10-15 cm apart and left to grow for 15-20 days in canals or for 45-60 days in ponds. *Gracilaria* is harvested in 6-12 months. Farmers usually start culture in June-July although some opt to start it in November-December.

Farmers do not harvest all the seaweed. About one-third is left to serve as seedstock for the next cultivation period. Farmers who plant in canals have 16-24 croppings in one farming period; pond growers, 12-16. The harvest is sundried for one day using old fish nets and bamboo slats. Dried seaweeds are packed in sacks (1 sack = 25 kilograms) and stored in warehouses for 2-3 months to accumulate a bigger volume and await a higher price.

Fresh harvest is sold to traders or in local public markets at P3-4 per kg. Dried ones is sold to traders at P7 per kg. Traders in turn sell them to exporters or processors. Canal farming yields 7-14 tons of dried seaweeds per hectare per year or an average of 1.3 tons per ha per crop. Pond farming produces 3-4 tons of dried seaweeds per ha per year or an average 450 kg per ha per crop.

Farmers initially invest P4,600 for a 1-ha canal or P16,000 for a 1-ha pond. This covers pond development, drying platform, dug-out, non-motorized banca, and working capital for the first cropping. Investment for succeeding crops is about P1,450 per hectare per crop for canal culture and P1,500 for ponds. This includes family labor, caretaker's salary, hired labor, marketing expenses, land tax, permit, and depreciation.

Farmers get a higher income from canal culture (P41,800 for 8 croppings) than from ponds (P24,350). Some of their problems include low



market price, predation, presence of associated algae, theft, no accessible market outlet, and poor farming technology.

Gathering seaweeds

A survey was conducted by SEAFDEC in 12 coastal municipalities of western Visayas to determine the seaweed gathering practices of fishermen. There were 83 gatherers involved in this small-scale industry, who live below the poverty line and who consider it as the number one minor source of income. Only seaweeds of value are gathered in big volume.

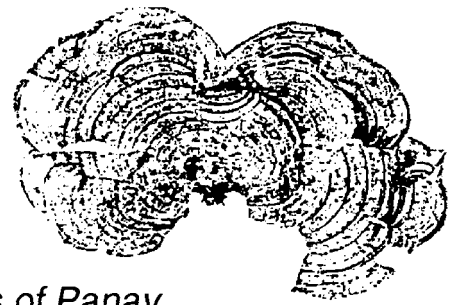
The seaweeds are gathered mostly in sandy-muddy, rocky, and sandy-rocky substrates. Most gatherers use their bare hands although some use tools. There were approximately 114 tons per year of seaweeds harvested from natural stock with a market value of ₱415,000. The harvest are as follows:

- 99.5 tons of the agarophytes *Gelidiella*, *Gracilaria*, and *Graciliariopsis*
- 10 tons of the carrageenophytes *Eucheuma* and *Kappaphycus*
- 10 tons of the table vegetable *Caulerpa*

Seaweeds gathered measure <50 to 200 cm in length. Gatherers pick the seaweeds in March, November, and April. Collection is daily, 3x, 2x, and once a week during low tide. Collection lasts 3-4 hours a day. Harvest seaweeds are sun-dried by spreading on the ground or sand, cement, bamboo slats, old fish nets, and dry leaves. Drying time is 1-2 days for *Gracilaria* and *Gelidiella* and three days for *Kappaphycus* and *Eucheuma*.

An average maximum income of ₱5,600 per gatherer per season is derived from seaweed gathering.

Excerpted from recently published SEAFDEC studies: (1) AQ Hurtado-Ponce, GPB Samonte, MRLuhan, N Guanzon Jr. 1992. *Gracilaria (Rhodophyta) farming in Panay, Western Visayas, Philippines*. *Aquaculture* 105: 233-240. (2) AQ Hurtado-Ponce. 1992. *Cage culture of Kappaphycus alvarezii var. tambalang (Gigartinales, Rhodophyceae)*. *Journal of Applied Phycology* 4: 311-313. (3) AQ Hurtado-Ponce, MR Luhan, N Guanzon Jr. 1992. *Gathering of economically important seaweeds in western Visayas, Philippines*. *The Philippine Scientist* 29: 40-47.



Seaweeds of Panay

The monograph published by SEAFDEC/AQD in 1992 lists the species of seaweeds found in Panay and Guimaras Islands in April 1988 to February 1989. Common names, descriptions, habitats, economic importance, and collection sites are given for 100 species of green, brown, and red algae, 41 of which are new records for Panay. (The *Padina minor* illustrated above, for instance, is a good source of algin and is used as fertilizer and fodder.)



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Seaweeds in medicine and dentistry

The agar from seaweeds is a good **laxative** and an important component of **hydrogel wound dressing**.

Alginates and alginic compounds can treat **heartburns**, prevent **gastroesophageal reflux**, control **bleeding**, act as **demulcent**, and are used in **obstetrics-gynecology**.

Agar and alginate are used as impression materials in **dentistry** or to fabricate cast inlays, onlays, and crowns.

To follow developments in seaweed research and the seaweed industry, subscribe to **SICEN Newsletter** published twice yearly by the Seaweed Information Center (SICEN) based at the University of the Philippines - Marine Science Institute. SICEN was established through a grant from the International Development Research Centre (IDRC) of Canada. The newsletter on seaweeds was first issued in February 1990; it is edited by Edna G. Fortes. Subscription is free. Write to: SICEN, College of Science, UP Diliman, Quezon City 1101.

Farming notes

(with reference to folk medicine and horticulture on pages 6-7, this issue)

Grouper, rabbitfish and oysters

The grouper *Epinephelus coioides*, the rabbitfish *Siganus guttatus*, and the oyster *Crassostrea* spp. are among the 20 or so commodities prioritized for research at SEAFDEC/AQD for 1995-1997. Accomplishments in their farming techniques are discussed in the ADSEA proceedings edited by Bagarinao and Flores (see page 22, this issue).

For the grouper, work on these areas still have to be done: (1) refinement of broodstock management and breeding techniques, (2) studies on reproductive biology and endocrinology, (3) improvement of hatchery and nursery techniques with alternative live food and water management, (4) studies on sources of wild seed, (5) improvement of holding and transport techniques for wild juveniles, (6) determination of nutrient requirements, (7) feed development for nursery and grow-out, (8) health management, (9) documentation and improvement of existing culture techniques, and (10) economics of monoculture and polyculture.

For rabbitfish: (1) refinement of broodstock management, (2) feasibility studies for searanching, (3) market study and socioeconomic assessment of existing industry, (4) cage culture as alternative livelihood, and (5) collation of traditional knowledge on rabbitfish biology, fishery, and culture.

For the oyster: (1) spatfall forecasting, (2) evaluation and refinement of culture technology, (3) transplantation and transfer of culture technology, and (4) product development.



The giant clams

All seven known species of giant clams are found in the Philippines. However, only the smaller attached species *Tridacna crocea*, *T. maxima*, and *T. squamosa* are widely distributed. Of the four unattached species, only *Hippopus hippopus* occurs in some numbers while the other three, *H. porcellanus*, *T. derasa*, and *T. gigas* are virtually extinct due to overexploitation.

Both shell and meat are utilized although the shell is a more important commodity. All species are harvested with women playing an equally important

role as the men. The clams are harvested from reef areas which are common property, without any management program at present.

Research on giant clams in the Philippines is undertaken principally by two institutions:

- Silliman University Marine Laboratory in Dumaguete City and
- University of the Philippines Marine Science Institute in Bolinao, Pangasinan

Studies have included resource surveys, growth, and mariculture. These research programs are part of a larger program that include the James Cook University in Townsville, Australia, the University of Papua New Guinea, and the Ministry of Primary Industries in Suva, Fiji. It is supported by the Australian Centre for International Agricultural Research.

Mariculture. Raising laboratory-reared clams in ocean nurseries was tested in 7 sites but most successfully in Pamilacan (an island southwest of mainland Bohol) in central Visayas. The ocean nursery in Pamilacan was within an established marine reserve, inside the reef, which is a mixed seagrass community. The site is partially protected from the monsoon trade winds, which can destroy cages, overturn clams, and chip off shells. *H. hippopus* juveniles (<12 to 14 months old) were placed in a simple fence-like enclosure of nylon net held in place by ipil-ipil or bamboo posts. Survival after 17 months was about 74%; remaining clams grew an average 3.65 mm each month.

Further reading: JW Copland and JS Lucas. 1988. **Giant clams in Asia and the Pacific.** ACIAR Monograph No. 9. 274 pages. (This monograph describes the research conducted by Silliman University and the University of the Philippines, among others.)



The marine turtles

In the Philippines, marine turtles now face a threat to their survival. They are hunted in the sea or slaughtered on the beach as they lay their eggs. The eggs and meat are taken as food while their skins and shells are processed into various by-products.

The government has prohibited the trade of marine turtles or its by-products; regulates the egg collection of communities that have traditionally depended on marine turtles as source of food; declared sanctuaries in Tawi-tawi (the Turtle Islands), Palawan (El Nido, Bacuit Bay), and Antique (Caluya); and deputized provincial officials as conservation officers or game wardens.

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Marine turtles live up to 60 years or more. At maturity, the males develop more elongated, curled claws and much longer tails than females. Marine turtles are air-breathing although they can dive for long periods and can swim powerfully. They have no teeth and use a sharp, horny beak and jaws to tear and bite their food. Their senses of sight, taste and touch are well-developed. Due to the absence of vocal cords, the only sounds they can make are hissing, grunting noises while exhaling, usually during courtship and mating.

Of the eight species of marine turtles occurring worldwide, five are present in the Philippines. One species is the green turtle *Chelonia mydas*. The green turtle derived its name from the color of its fat. It has many names in the local dialect but is more popularly called **pawikan** (Tagalog). Adult females measure 54-121 cm carapace length and weigh 113-182 kilograms. It is carnivorous during its first year of life, becoming exclusively vegetarian when adult. Algae and seagrasses are its favorite diet.

The Department of Environment and Natural Resources (DENR) notes that many gaps still exist in the study of marine turtle biology and ecology. So far, only the nesting process of marine turtles has been studied extensively. DENR also maintains hatcheries to protect eggs against poachers and predators during their incubation period. These eggs are collected from beaches. Approximately 500,000 marine turtles have successfully emerged from these hatcheries and have been released to the sea.

DENR enjoins all to contribute and support marine turtle conservation:

- do not kill or injure marine turtles
- do not use dynamite or cyanide when fishing
- do not gather marine turtle eggs
- do not litter or throw garbage in their habitat
- do not buy or sell turtle eggs, turtle meat, stuffed turtles and its by-products such as guitars, combs, bangles, earrings, and rings
- report people engaged in these illegal activities to the authorities
- if you see a turtle with a metal tag in its front flippers, write down the serial number and species, the date and place the turtle was spotted. Never remove the tag; the turtle may be spotted somewhere else and this would help in the research on migratory routes. Send this information to: Pawikan Conservation Project, Protected Areas and Wildlife Bureau, NAPWNC, Quezon Avenue, Quezon City 1100.

Further reading. Marine Turtles in the Philippines produced by the DENR. 10 pages.



The "killer" crocs

The fear of crocodiles seems universal, especially for saltwater species that are known to attack humans. Freshwater species has no such record. Crocodiles are among the oldest creatures on earth, having survived 200 million years. They are important in regulating the food chain in aquatic ecosystems, and their feces is known to spur the growth of plants that are eaten in turn by fishes. They are protected under the Convention on International Trade in Endangered Species of which the Philippines is a signatory.

The Crocodile Farming Institute is a joint project of the Governments of the Philippines and Japan through the DENR and the Japan International Cooperation Agency. It is based at Barangay Irawan, Puerto Princesa City in Palawan. The Institute aims to conserve two endangered species of crocodiles -- the Philippine crocodile *Crocodylus mindorensis* and the Indo-Pacific *Crocodylus porosus* -- and to develop farming technology for local communities. By the end of 1992, its croc population had reached almost 1,500 of which 90% were bred in captivity. The Institute believes in the potential commercialization of crocs as a dollar-generating industry given the prevailing prices of its hides (\$8 per cm² in the world market) that are used to manufacture bags and shoes. Its meat is also considered a delicacy in some countries. Farming crocs has been a profitable venture in Thailand, Australia, and Zimbabwe for several decades.

The Institute built a prototype backyard croc farm inside the institute's 10-hectare complex. The structure is worth ₱18,000 and consists of three adjoining bamboo pens with concrete pools in the middle surrounded by compact soil. The biggest pen is a 25 m² enclosure 5 ft high fitted with iron sheets all around as an added precaution.

In 1993, the Institute began pilot testing its community-based farming technique. It provides 25 crocs, each about a year old, to qualified cooperatives who raise the crocs for three years. Breeders provide enough food (leftover fish or meat unfit for human consumption) and water.

Farming crocs is intended to be a sideline (the breeder spends two hours a day to care for them). A breeder can earn ₱77,000 net in three years (US \$1- ₱25).

The Institute publishes a quarterly publication **CFI News**. Send requests to RP-Japan Crocodile Farming Institute, PO Box 101, Puerto Princesa City 5300, Palawan.



Sea urchins and company

The University of the Philippines in the Visayas pursue research on economically important echinoderms (sea urchins, sea cucumbers) in its Marine Biological Station within the DENR's Taklong Island National Marine Reserve in Nueva Valencia, Guimaras. Since the late '70s, more than 40 studies have been completed on reproductive biology of echinoderms as well as in marine biodiversity, coral population biology, soft coral toxicology, mangrove, seagrass, reef ecology. Mariculture of echinoderms were also undertaken.

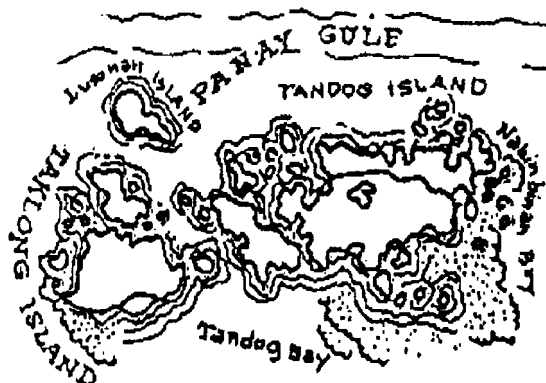
The Station is the University's support arm for instruction in the aquatic sciences, for coastal ecology and marine resources management research and for its extension activities. The University plans to develop the station into a Center for Coastal Marine Studies and Resource Management and to establish a marine park within the reserve for environmental education and stewardship.

For more information, write to: Dr. James L. Torres, Chairman/Division of Biological Sciences, College of Arts and Sciences, UP in the Visayas, Miag-ao 5023, Iloilo.

Bioactive compounds from marine plants and animals. The University signed a Memorandum of Agreement with Nova Sciences, a company engaged in the commercial development of biological products for food and pharmaceutical industries. Nova Sciences has a major research project directed to identify bioactive compounds from marine plants and animals. A research laboratory will be established in the University's Miag-ao campus in Iloilo. Proposals have been prepared for studies on barnacles, *Gracilaria* and fishes like the African catfish.

Biotechnology. A National Institute of Biotechnology for Aquatic Science will be established with UP Visayas as the lead institution. The Institute is mandated to develop techniques for goods and services related to food and aquatic resources. The Institute will:

- isolate, purify, characterize, identify, and synthesize bioactive substances from aquatic organisms
- develop and improve the breeds of aquatic species with commercial importance through



UP Visayas maintains a marine station within a reserve managed by the Philippine government 12°E 10°N

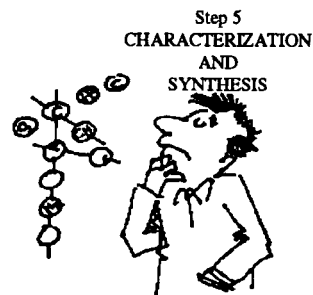
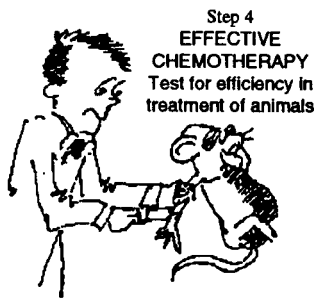
- monosex culture, polyploidy production, eugenics and transgenics, recombinant DNA technology
- improve culture techniques to maximize production through biocontrol
- produce diagnostic tools and rapid detection methods
- establish fish and crustacean cell lines, hybridoma, and plankton culture
- pursue pollution control through bioremediations, waste treatment and utilization
- synthesize bioactive compounds using fermentation technology
- pursue taxonomic studies on prokaryotes and eukaryotes including their culture

Updates of the University's activities are published in the **Otolith**, the quarterly newsletter of the College of Fisheries. **Otolith** was first issued in September 1994. Write to: The Editor, Otolith/College of Fisheries, UP Visayas, Miag-ao 5023, Iloilo.

Microbiology convention. The Philippine Society for Microbiology Inc. with UP Visayas, PHILAB Industries Inc., and QUALIMED Enterprises is convening its First Annual Convention on 26-27 October 1995 with the theme "Microbiology and Biotechnology Towards the 21st Century." The convention will be held at UPV. Contact the convention secretariat: PSM Visayas Chapter, UPV Division of Biological Sciences, Miag-ao.

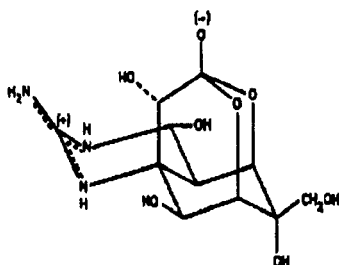
Among the papers to be presented are on the antimicrobial activity of aqueous extracts from selected Philippine soft corals (by RA Aguilar and MF Nievaes) and on the antifungal activity of akapulco *Cassia alata* leaves (RB Pareñas and MV Gacutan). Write the authors, c/o the UPV Division of Biological Sciences, for more information.

Some marine toxins

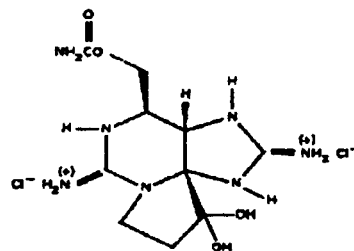


Tetrodotoxin: puffer-fish toxin

Ancient writings especially in China and Japan have referred to toxic puffer-fishes (Tetraodontidae). The Chinese book **Sankaikyō**, written about 2,000 years ago, describes the death of a man who ate puffer-fish intestines. The initial symptom includes paralysis of the tongue and lips that occurs in about 20 minutes to 3 hours and is progressive. Death occurs in 6-8 hours. The toxin is present in most tetraodontid species (about 29 in Japan), approximately half of which are edible. *Fugu* for example is an expensive delicacy. As the toxin is concentrated in the intestines and skin, the art of preparing *fugu* lies in removing these without contaminating the rest of the fish. Stringent regulations for handling *fugu* were introduced during the Edo period (1603-1868), and in Japan today all cooks must pass an examination on its preparation before they can serve *fugu*.



Tetrodotoxin (left) isolated from the pufferfish, and **saxitoxin** (right) isolated from the microscopic red algae which cause "red tides", are extremely toxic and block the transmission of nerve impulses. They have been widely used in neurophysiological research.



The toxin in puffer-fish is tetrodotoxin, one of the most poisonous non-protein toxins known to man (LD₅₀ about 10 μg/kg in rats). Attempts to isolate the toxin date back to 1909, and it was not until 1964/65 that its structure was established by three research teams working independently of each other. The long wait was not in vain; tetrodotoxin has a previously unknown structural characteristics. It is a neurotoxin that inhibits the transmission of nerve impulses by selective

blockage of sodium ions. It is widely used in neurophysiological research on the mechanisms regulating nerve impulses. Tetrodotoxin has also been used in clinical medicine; in Japan it is used as a muscle relaxant and as an analgesic in the treatment of certain tumors.

Saxitoxins: paralytic shellfish poison

Another cause of food poisoning in humans is found in mussels and shellfish. The toxin comes from red microalgae (dinoflagellates) that mussels and shellfish ingest. The toxin concentrates on their bodies, and in turn they become toxic and inedible. Paralytic shellfish poison poses a very serious problem in the United States and Canada, as the puffer-fish does in Japan. There are similarities between the poisons -- they have both caused many deaths, they produce very similar symptoms and the causative agents are highly toxic and act in much the same way. The

first toxin to be isolated was saxitoxin obtained from an edible bivalve, the *Saxidomus giganteus*. Its structure was established in 1975 by Shantz and his collaborators, after more than 20 years of research.

Palitoxin: the most toxic marine product

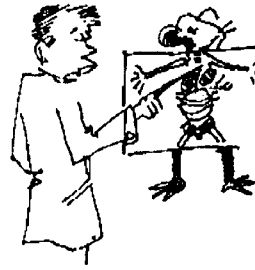
Palitoxin is isolated from a zoonthurian *Palythoa toxica*. An ancient Hawaiian legend

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Step 6
MASS SCALE
SYNTHESIS



Step 7
PHARMACOLOGICAL
STUDIES
Testing for drug
activity and safety



Nereistoxin

The toxic principle of the marine annelid was first studied in 1922 by Nitta, who was fascinated by the observation that a patient who handled the worms complained of respiratory abnormality, headache, and vomiting. Nitta isolated a crystalline toxin named nereistoxin in 1934.

Nereistoxin is an unusual amine having a 1,2 dithiolane ring that is rare in natural products. Its chemical formula is $C_5H_{11}NS_2$. Qualitatively, the toxin gave reactions similar to those of thioctic acid.

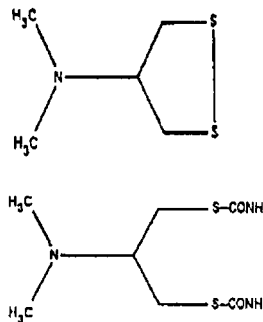
Pharmacology

Nitta tested the effects of nereistoxin in animals including mammals, birds, reptiles, and fish. He concluded that nereistoxin primarily affects the nervous system. The lethal dose that could kill 50% of a given mice population (LD_{50}) is about 30 mg/kg intravenously, 1,000 mg/kg subcutaneously, and 118 mg/kg orally. Nereistoxin is apparently not potent. It does not affect killifish and goldfish although its toxicity is enhanced by alkaline water pH. Then it can cause paralysis and eventually death. At water pH below 5.6, nereistoxin is not toxic.

In extensive electrophysiological studies, it was discovered that nereistoxin blocks synaptic transmission in the central nervous system. But its inhibitory action on cholinesterases (a type of enzyme) is not enough to kill insects. In cockroaches, nereistoxin suppresses excitation of the abdominal nerve bundle or of the postsynaptic potential, but not all of the tail hair nerve. Since nereistoxin competes with added acetylcholine (an excitatory transmitter substance) in contraction of the frog skeletal muscle, the toxin probably blocks the synaptic transmission by competing with acetylcholine at a postsynaptic membrane receptor site of the central nervous system (CNS).

When an insect is intoxicated by nereistoxin, stimulation from inside or outside the body is not adequately transmitted to the CNS. Thus, disturbance of a CNS-mediated function results in softening of the body, loss of response, among others. The effect is complete relaxation and anesthetization of the insect.

Application in agriculture



Nereistoxin (top) was isolated in the worm *Lumbriconereis heteropoda*, and has been used as a model for the synthesis of **Padan** (bottom), which is employed as an insecticide in Japan.

Nereistoxin possesses potent insecticidal activity, particularly to the larvae of the rice stem-borer. Researchers synthesized a number of compounds with a structure similar to nereistoxin. The most effective -- 1,3-bis-(carbomolico)-2-N, N-dimethylamine propane -- was patented and used in agriculture since 1967. Application had been extended to the rice plant skipper, the white tip rice nematode, the cabbage worm, the tea leaf roller, the green elongated leafhopper, the citrus leaf miner, the persimmon fruit moth, and others.

References: (1) Yoshiro Hashimoto. 1979. **Marine toxins and other bioactive marine metabolites**. Japan Scientific Societies Press, Tokyo. pp. 302-309. (2) Luigi Minale. 1985. *Medicine from the sea*. In: SG Richardson (ed). **Managing the Ocean; Resources, Research, Law**. Lomond Publications Inc. Maryland 1985.

The Philippine Bureau of Food and Drugs

The Bureau of Food and Drugs (BFAD) under the Department of Health was established to administer and enforce regulations that would ensure the safety, efficacy, and quality of processed foods, drugs and cosmetics, diagnostic reagents, medical devices, and household hazardous substances.

BFAD does the following:

- inspect and license establishments such as manufacturers, traders, distributors, importers, exporters, wholesalers, and retailers
- evaluate, test, and register products
- ensures the quality and truthfulness of information about these products in labels, advertisements and promotional materials by approving product label prior to commercial distribution and by monitoring advertisements and promotional materials

To pursue their mandates, BFAD cooperates with the Japan International Cooperation Agency, World Health Organization, Association of Southeast Asian Nations, Food and Agriculture Organization, United States Pharmacopeia Convention, and the United States Food and Drug Administration.

Generics Act of 1988

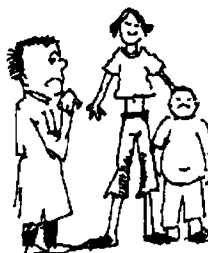
The Philippine Government ensures that safe and effective drugs are available to all Filipinos at any time and place and at reasonable and affordable cost.

The government promotes, encourages and requires the use of generic names for all drugs that are imported, manufactured, advertised, prescribed, or dispensed. A generic name is a simple term for the scientifically recognized active ingredient of a drug. For example: paracetamol is a medicine that controls fever; it is the generic name for N-acetyl-aminophenol. Brand names of paracetamols include Temptra, Biogesic, and Tylenol. The use of generic names reduces the cost of treatment because it lowers the promotion and advertising costs associated with brand name drugs.

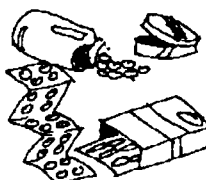
Available and affordable drugs have always been a problem. The local market is flooded with 12,000



- Step 8
GOVERNMENTAL APPROVAL
- Disclosure of complete drug source and manufacturing information
 - Preclinical results disclosed
 - Future research plans and other supporting data



- Step 9
CLINICAL EVALUATION
- Testing with human volunteers to determine metabolism, absorption and elimination, side effects, safe dose range, preferred method of administration.
- Obtain therapeutic index (value versus hazards).
- Initial diagnosis test
 - Outside controlled tests



- Step 10
MASS PRODUCTION
- Economic, governmental, technical limitations apply



- Step 11
MARKETING PROCEDURES
- Economic, governmental, technical limitations apply

different drugs, many of these are of dubious quality and most are beyond the means of most consumers. And yet, 90% of all ailments can be cured by 250 drugs (termed essential drugs) already in the market, says the World Health Organization (WHO). These essential drugs must be available and affordable to all citizens. Only drugs included in a List of Essential Drugs and a Complementary List of Drugs can be marketed in the Philippines. These are drugs officially recognized by the government based on the WHO concept. The list will eliminate drugs of dubious nature.

The Philippine Government is the single biggest buyer and user of pharmaceutical products.

Sources: (1) Primer on the National Drug Policy by the Department of Health. (2) Republic Act No. 6675.

Future drugs from the sea

Several marine chemicals are likely candidates for future drugs. Here are a few being explored by US scientists.

- **Discodermolide** from the Bahamian sponge *Discodermia dissoluta* is a powerful immunosuppressive agent that may have a future role in suppressing organ rejection after transplant surgery.
- **Bryostatin** from the West Coast bryozoan (moss animal) *Bugula neritina* and **didemnin B** from a Caribbean tunicate of the genus *Trididemnum* are both in clinical trials as cancer treatments.
- **Pseudopterosin E** from the Caribbean gorgonian coral *Pseudopterogorgia elisabethae* and **scaladial** from dictyoceratid sponges found in the western Pacific are both being studied as anti-inflammatory agents.
- **Dolasstatin** from the sea hare *Dolabella auricularia* and **ecteinascidin** from the tunicate *Ecteinascidia turbinata* have pending clinical trial application as anti-cancer compounds.
- **Halichondrin B** from the sponge *Lissodendoryx* (and others) and **halmon** from the red algae *Portieria hornemannii* have reached preclinical trial stage as anti-cancer compounds.

Other marine chemicals are being investigated in Europe and in Japan, but we know less about the progress of these studies. There ap-

pears to be no shortage of marine chemicals that are potential candidates for drugs. The problem is that so many chemicals show promising activity in the initial screens that it is very difficult to predict which will become truly significant discoveries.

It seems inevitable that economic considerations will prevent the development of many marine chemicals that are very effective but

difficult to obtain. The rise and fall of interest in marine prostanoids clearly illustrates this. Prostaglandins are important human hormones that control blood pressure, renal blood flow, contractions of smooth muscle, and gastric acid secretion, and are involved in inflammation. When prostaglandins were first isolated from sheep seminal tissues, these were difficult to obtain in even

The discovery of a new drug from an organism's molecular structure will not mean a mass harvesting of the oceans. Scientists will eventually culture the organism or synthesize its molecular structure in the laboratory.

- Dr. Paul Scheuer, University of Hawaii
Makai 15(7) July 1993

minute quantities and were extremely expensive. When closely related chemicals called prostanoids were acquired in substantial quantities from the Caribbean gorgonian coral *Plexaura homomalla*, there was a rush to harvest gorgonians, isolate the prostanoids, and convert these chemicals into biochemically active prostaglandins. Within a year, however, prostaglandins were being produced by laboratory synthesis, and the marine prostanoids were soon forgotten, much to the relief of those who value the shallow reef environment's natural beauty. This episode provided a valuable lesson for entrepreneurs seeking new pharmaceuticals

☞ p. 20

High-profile cases in Philippine media



Halichondrin B and halmon

Astonishing new drug discoveries from the sea's diverse plant and animal life forms are currently being uncovered by scientists for treatment against cancers, the US Journal of the National Cancer Institute revealed recently.

This include the "halichondrin B" from Pacific sponges and "halmon" from red algae found off the coast of the Philippines.

The latest issue of Health Horizons, a publication of the International Federation of Pharmaceutical Manufacturers Association (FPMA), noted that scientists are encouraged due to a finding that 30% of the organisms beneath the sea showed cytotoxicity (capacity to kill cells) and that 7% were active against leukemia, cancer of the blood.

It said that some 1,000 organisms ranging from coral to algae and starfish are found every year. These are frozen and their extracts are tested on 60 cancer cell lines. The extracts are not thawed but are chipped and minced before study, scientists reported.

The scientists noted that very few marine organisms have yet been studied intensively and less than one tenth of the seas have been surveyed.

One compound from a sponge found in Canadian waters was found to be more potent than the widely used adriamycin. The compound is being synthesized because the sponge is rare.

Important active compounds from marine organisms have already been isolated and fully synthesized by the pharmaceutical industry like cytosine arabinoside and adenine arabinoside as medicines for cancer and viral herpes.

Tube-like spineless creatures from the

Caribbean have been discovered too. These yielded chemicals called didemin B which is presently being tested against brain, lung and prostate cancers.

Biochemical scientists have also found active compounds called "bryostatins" which are said to affect Kinase C that mediates the growth of cancer cells. These are in clinical trials in Europe and trials are planned in the United States.

Other compounds discovered for the ongoing cancer drug research are "dolastatins" from sea hares related to snails and limpets.

The US National Cancer Institute is currently very busy testing marine natural products from the South and Central Pacific, the Caribbean and Antarctic in search for new drugs.



Lumazine

The protein that gives deep-sea fish that eerie blue glow could someday help overcome the growing danger of drug-resistant bacteria.

Biochemist John Lee of the University of Georgia and colleagues think their work on bioluminescence could lead to a method of striking at disease-causing bacteria in a way drugs like penicillin can't. The lumazine protein of the deep-sea fish could provide a battle plan that invading bacteria can't defend against.

"My guess is that you could never get around this one," Lee said.

Other researchers called Lee's work a novel approach but cautioned that the jump to a new antibiotics is a long one.

Lee's target for attack is bacteria's factory for riboflavin - vitamin B₂ - which cells need to produce energy. "Throwing a monkey wrench in that

factory's works would kill the bacteria," he said.

Researchers have known about one of riboflavin's vulnerable spots, an enzyme vital for its production, but haven't been able to figure out how to get at it. The enzyme, called riboflavin synthase, has too many functions for scientists to easily knock it out of commission, Lee said.

That line of study has been all but abandoned. But when Lee's team recently unraveled the lumazine protein's structure, they found that it was startlingly like that of the enzyme, although much smaller.

"The two proteins are actually cousins," Lee said. "They apparently evolved from the same ancestor."

There's one important difference in how the two function. Unlike its cousin, the lumazine protein works by itself, not as part of a factory. Learning how to shut it down could lead to a way to "arm" the enzyme with another molecule and dismantle the riboflavin factory -- killing the bacteria.

"Now that we have two proteins, one of which is easier to understand, we'll focus on that one," Lee said.

As more kinds of bacteria grow resistant to antibiotics like penicillin and streptomycin, scientists are looking for drugs that use other methods to attack bacteria.



Red tide antidote

Toxicologists from the University of the Philippines are trying to develop an antidote to the red tide poison from carageenan or seaweed extracts. Results are promising.

Red tide poisoning kills one out of ten victims in the country. There are 113 cases since red tide (also called PSP or paralytic shellfish poisoning) surfaced in 1989. Red tide has already affected 19 provinces.

Doctors give PSP victims sodium bicarbonate or baking soda, active charcoal, and fluids for hydration. Dr. Irma Macalinao of the UP National Poisons Control Group said that the present treatment has saved many lives, particularly for patients who recognize PSP symptoms early enough. These symptoms include nausea,

diarrhea, difficulty in breathing, numbness of extremities, and tingling sensation in the face.

Toxicologists say they found less red tide toxins in test tubes with carrageenan. Apparently, seaweed extracts "attract" and eliminate the toxins.



Shark - answer to cancer?

Unlike bony fish, mammals and amphibians, sharks never get cancer.

Researchers say a mystery substance found in the cartilage inhibits tumor growth in rabbit eyes. The yet unidentified substance does not act directly on the tumor itself but deprives the cancer mass of its supply of blood, says scientists at the Massachusetts Institute of Technology. The substance resembles the protein extracted from cartilage of calves that also inhibits tumor growth.

Cartilage is the tough elastic connective tissue found around bones in mammals. In sharks, the skeleton is composed entirely of cartilage and not bone. Cartilage composes about 6% of the shark's total body weight, compared to less than 0.6% in calves. Some sharks are very large, about 10 times heavier than calves.

For calves, it takes 500 grams of cartilage to get one milligram of the extract; for sharks, only one-half gram is needed.

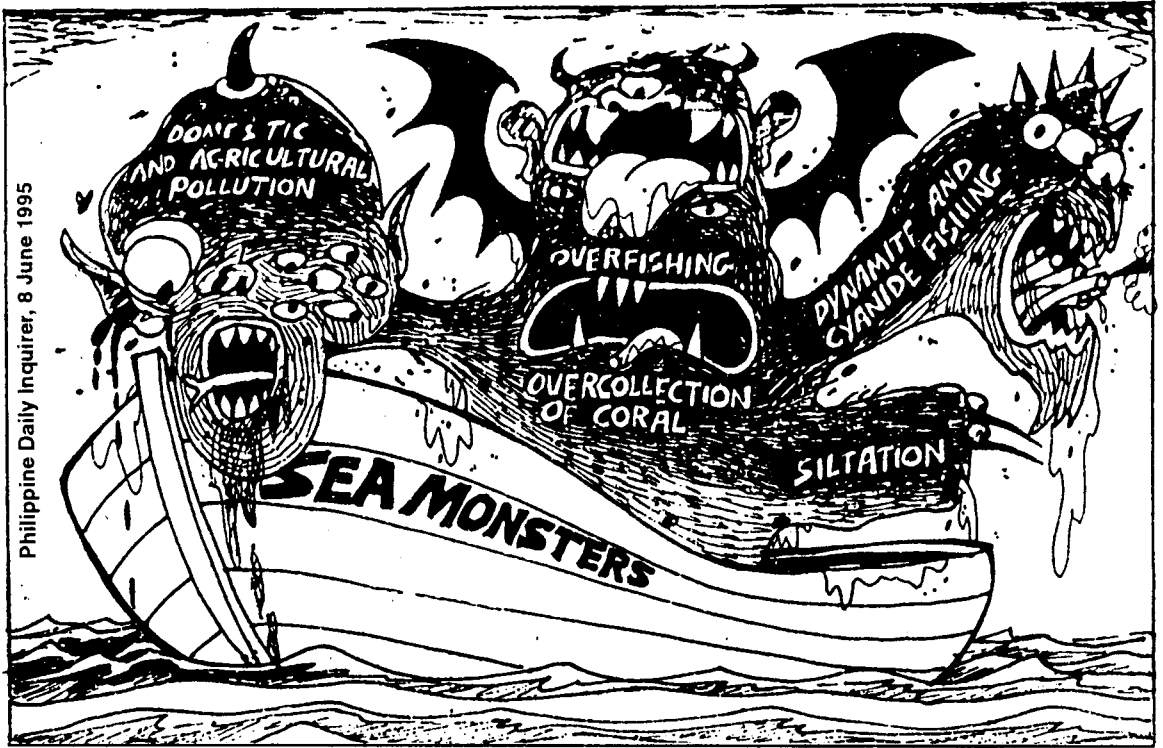


CD-ROM on drug research

A comprehensive information on hundreds of drug researches and developments is now packed on a CD-ROM for the perusal of all scientists

at health ministries, research institutes and pharmaceutical companies worldwide.

The new CD-ROM which is regarded as the world's foremost information system on drug development is produced by Pharma projects in England which is owned by PJB Publications, a pharmaceutical publishing company established by Dr. P.J. Brown of London.



SOME MARINE TOXINS ... FROM PAGE 14

describes a potent poison found in seaweed known as *limu-make-O-Hana* (the deadly seaweed of Hana). The islanders of old smeared the tips of their lances. It was not until 1861 that the habitat described in the legend was discovered and scientists were able to collect the seaweed. Moore and Scheuer isolated the toxin in 1971, and its structure was definitively established ten years later. Palitoxin has an unusual structure. Despite its great molecular weight (around 3,300 daltons), it is not formed by the repetition of simple structural units like polysaccharides. Palitoxin is extremely poisonous (LD₅₀ about 0.5 µg/kg in rats) and possesses antitumoral properties. A dose of around one-tenth of the minimum lethal dose completely cures Ehrlich's tumor in rats. It has recently been used as a local anaesthetic in maxillofacial surgery, allowing surgeons to operate for several hours at a time. It is a powerful vasoconstrictor and is potentially useful in the study of angina in animals.

Excerpted from: Luigi Minale. 1985. *Medicine from the sea*. In: SG Richardson (ed). *Managing the Ocean; Resources, Research, Law*. Lomond Publications Inc. Maryland 1985.

FUTURE DRUGS FROM THE SEA ... FROM PAGE 17

from marine organisms: We should expect marine chemicals to inspire new drugs rather than to provide them.

Chemicals from marine organisms have proved to be different from plant sources, and have provided valuable tools for biomedical research, as well as inspiration to the pharmaceutical industry. Biochemical studies have positively influenced marine biology, in as much as they have focused attention on marine invertebrates and led to pioneering research on invertebrate aquaculture and invertebrate-cell tissue culture. If we consider the 1980s to be a period of basic research on chemicals from marine organisms, then the 1990s will surely see new drugs and other chemical products that are inspired by this research. We will then have accomplished our goal of demonstrating the biomedical potential of chemicals from marine organisms without causing any lasting damage to the marine environment.

Sources: (1) *Oceanus*, 1992. *Oceanus* reports on research at the Woods Hole Oceanographic Institution. (2) *Science* Vol. 266. November 25, 1994.

Aquaculture clinic

QUERY Is there a book already published that collates all information on pharmaceutical products from marine sources?

REPLY Yes, there are books on marine pharmacology. Unfortunately, SEAFDEC/AQD does not actively collect information on this field being focused on aquaculture instead. Other than the references used in this issue, the few books the SEAFDEC/AQD Library has on marine pharmacology are quite dated now but are still useful as references. Three are abstracted below.

Marine Algae in Pharmaceutical Science

EDITED BY Heinz Hoppe, Tore Levring and Yukio Tanaka PUBLISHED BY Walter de Gruyter & Co. Germany 1979. 807 pp.

International seaweed symposia have always been a forum for those interested in marine algae, whether their taxonomy, morphology, ecology, physiology, cultivation, chemistry, biochemistry or application. The last in particular is the fruit of all other aspects of algal sciences.

Algae are potential sources of pharmaceutically and medically important substances. The monograph is a single-volume survey of current knowledge in this field.

Marine Pharmacology A Study of Toxins and Other Biologically Active Substances of Marine Origin

WRITTEN BY Morris Baslow
PUBLISHED BY The Williams and Wilkins Co. Baltimore 1969. 286 pp.

This work is the outgrowth of the author's interest in marine pharmacology and biochemistry and the presentation of a graduate course on marine pharmacology at the University of Hawaii.

The primary effort in this book has been to bring together results of investigations into the pharmacological potential of compounds derived

from marine organisms that are scattered throughout the literature. There are many excellent monographs and reviews of material on specific subjects, and in these the reader will be able to follow the development of past work in each field. In the book, all animal and plant phyla have been included, and all potential pharmacological agents considered. Non-marine organisms are considered in cases where related marine forms contain similar substances.

Marine Pharmacognosy Action of Marine Biotoxins at the Cellular Level

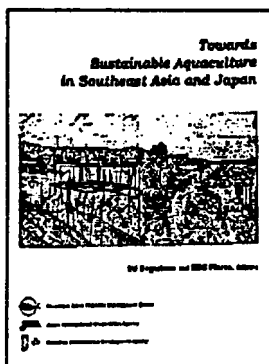
EDITED BY Dean Martin and George Padilla
PUBLISHED BY Academic Press New York 1973. 317 pp.

This volume provides comprehensive coverage of the use of bioactive compounds of marine origin as tools for studying cellular physiological processes. It brings together the research results of several investigations concerning the toxic effect of these compounds on cells. Equally important, it provides the reader with a number of readily applicable techniques for isolating and identifying these compounds, and for studying their physiological and pharmacological activity and relationship to known cellular functions. Included is a discussion of the general effects and potential usefulness of bioactive compounds in terms of their specific cellular action.

The opening chapter discusses the relationship of structure and function in bioactive compounds. Subsequent chapters examine new toxins derived from marine sources. The contributors are all internationally known specialists, who outline detailed methodologies and experimental procedures of great value to investigators seeking new means of assessing biological activity in marine biotoxins.

This volume will serve as a valuable source of current data and research procedures for cell and marine biologists, pharmacologists, toxicologists, biochemists, neurobiologists, zoologists, and oceanographers. It will be especially useful to students in these fields.

New publication



Towards Sustainable Aquaculture in Southeast Asia and Japan

EDITED BY T.U. Bagarinao
AND E.E.C. Flores
PUBLISHED BY SEAFDEC/AQD
1995; 254 pages

This proceedings volume documents the presentations at ADSEA '94, the third Seminar-Workshop on Aquaculture Development in Southeast Asia. ADSEA '94 included reviews of the status of aquaculture development in Southeast Asia and Japan and of the research conducted by SEAFDEC/AQD to contribute to this development. Invited scientists then talked on various topics including responsible aquaculture, mollusk and seaweed culture, integrated farming, shrimp culture, diseases and health management, and transgenic fish.

The volume also lists the priority research areas of 20 or so commodities at SEAFDEC/AQD in the next three years (1995-1997). Research programs are now directed to the generation of aquaculture technologies that are economically feasible, environment-friendly, and socially equitable.

ADSEA '94 was convened with funding support from the Japan International Cooperation Agency and the Canadian International Development Agency.

Meeting on the Use of Chemicals in Aquaculture in Asia

20-22 May 1996
Tigbauan, Iloilo, Philippines

The meeting will synthesize all information related to the use of chemicals in aquaculture. It will review the use of antibiotics with special emphasis on their use as therapeutants; ecological effects of chemical use in aquaculture; generation of drug resistance in sediments and soils, tissues, and water; use of chemicals in aquafeeds; human health aspects in aquaculture with emphasis on food safety and food quality assurance; regulations on chemical use in aquaculture; and the use of organic manure, fertilizers, and conditioners. Information on chemical use in these countries will be discussed: China, Indonesia, Japan, Malaysia, Singapore, the Philippines, Taiwan, Thailand, Viet Nam, Cambodia, Laos, Bangladesh, India, and Pakistan.

The recommendations of the Meeting will be directly fed into the Meeting of the Working Group on Environmental Impacts on Coastal Aquaculture of GESAMP (the IMO/FAO/UNESCO-IOC/WMO/IAEA/UN/UNEP Joint Group of Experts on the Scientific Aspects of Marine Environment Protection) that will follow the Meeting at the same venue.

The meeting is organized by SEAFDEC/AQD and FAO's Inland Water Resources and Aquaculture Service with financial support from SEAFDEC, FAO, and CIDA and the cooperation of the Network of Aquaculture Centres for Asia and the Pacific, Japan International Research Center for Agricultural Sciences, Taiwan Fisheries Research Institute, and ICLARM.

Please address all correspondence to: Ms. Celia L. Pitogo/Chair, Local AQUACHEM Organizing Committee, SEAFDEC/AQD.

Training courses for 1996

TENTATIVE SKED

Aquaculture Management	26 Mar - 24 Apr
Fish Health Management	16 Apr - 28 May
Marine Fish Hatchery	3 June - 23 July
Coastal Aquaculture	31 July - 27 Sept
Freshwater Aquaculture	5 Sept - 16 Oct
Shrimp Hatchery Operation	1 Oct - 20 Nov
Fish Nutrition	23 Oct - 3 Dec

For application forms and further information, please contact: TRAINING AND INFORMATION, SEAFDEC/AQD.



Second International Conference on the Culture of Penaeid Prawns & Shrimps

14-17 May 1996
Iloilo City, Philippines

The conference will review researches of the past decade, identify research gaps, and propose strategies to make the shrimp industry sustainable. Emphasis will be on genetic resources, environmental impact, emerging grow-out and culture techniques, and socio-economic and management aspects of culture operations. Shrimp physiology, nutrition, and diseases will also be discussed.

Registrations received before 15 January 1996 are discounted.
Contact: SECRETARIAT,
SICCPSS, SEAFDEC/AQD.

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To our valued readers:

In the past two years, you must have noticed a few changes in our newsletter. The regular editor Mila Castañón was joined by three other editors -- Julie Lagoc, Eva Aldon and Auggie Surtida -- who bring their own personal style to the AFN. We wanted to work on several issues simultaneously to hasten production and to allow our staff time off for travel and training. Mila, for example, went to Canada for an eight-month training on environmental technology (communication focus). Eva trained a year earlier. Auggie went to Thailand for a two-week staff exchange agreement with the SEAFDEC Secretariat. Julie frequently visits her children in the USA. **AFN** will have guest editors for a few more years to keep it interesting and timely.

Did you also notice the change in the masthead earlier this year? We added the SEAFDEC logo. This is in line with the corporate look the Center is building up. Whatever else you might have noticed, if you like it or not, don't hesitate to let us know.

AFN can now be accessed worldwide. Look us up in **Fisheries Review**, the indexing volume provided by the National Biological Service (NBS) under the United States Department of Interior (USDI), America's principal conservation agency. **Fisheries Review** contains indices of current literature in fisheries research and management. NBS-USDI first indexed the 1993 issues of **AFN** edited by Mila Castañón [**Fisheries Review** 39 (3, 4) 1994]. These issues include **Milkfish Breeding**, **Tilapia Culture**, **Policing Fisheries in the Philippines**, and **Catfish Culture**. **Fisheries Review** 40 (2) 1995 indexed the 1994 issues of **AFN** — **Farming the Sea** and **Hatchery Systems** edited by Mila Castañón and **Alternative Development** and **Conserve Biodiversity** edited by Julie Lagoc.

We are quite proud of the indexing because it puts **AFN** on the map, so to speak. Our circulation had always been limited — about 2,500 copies per issue and mostly in the Philippines — and being indexed in a world-wide database increases our "circulation" a million-fold. We are also proud of the progress **AFN** made since its inception in 1978. It started as a source sheet for local radio broadcasts; now, it is recognized as a full-fledged newsletter. We have the previous editor-writers (now resigned) to thank for starting the newsletter: Pedro Bueno, Rafael Lapastora, Nicanor Primavera, and Alexandrina Benedicto-Dormitorio. We also get lots of help from the AQD Library that houses the most recent information on aquaculture in Southeast Asia and the latest in literature search facilities (CD-ROMs).

The editors are not alone in putting the **AFN** together. Beginning the last issue before 1983, **AFN's** technical accuracy (and that of all books produced by AQD) was reviewed by a Publications Committee chaired by Jurgenne Primavera. Other chairs include Enrique Avila, Irineo Dogma Jr, Gerald Quintino and Teodora Bagarinao.

We sometimes see **AFN** in the **Ichthos** newsletter of JBL Smith Institute of Technology (South Africa). The work of our artists Ed Ledesma and Sid Tendencia gets reprinted. Two years ago at the ADSEA seminar in Iloilo City, UNDP/FAO's Imre Csavas noted that **AFN** serves a unique function in putting together information on certain topics. Local demand for back issues has been encouraging. For instance, Governor Juan Frivaldo of Sorsogon ordered 500 copies more of **Policing Fisheries** for fishermen cooperatives in his province. Indeed, we welcome any requests for information found on **AFN**. Write the **AFN Editor**. We hope you will continue to find **AFN** useful and informative.

— AFN PRODUCTION STAFF

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AFN is a production guide for fishfarmers and extension workers. It discusses the technology for cultured species and other recent information excerpted from various sources.

In citing information from AFN, please cite the institutional source which is not necessarily SEAFDEC/AQD. Mention of trade names in this publication is not an endorsement.

Editor: M. Castañón; Production: D. Badilles, R. Buendia, E. Ledesma, L. Plondaya, J. Requintina, I. Tendencia, E. Gasataya; Circulation: R. Tenedero, L. Tabigo-on, Jr.

Subscription rate: P40 per year (local), US\$ 15 per year including air mail postage (foreign). Please make remittances in postal money order, bank draft, or demand draft payable to SEAFDEC/AQD.

Aqua Farm News is published bimonthly by the Aquaculture Department of the Southeast Asian Fisheries Development Center P.O. Box 256 Iloilo City 5000 Philippines

Entered as second class mail matter at PPC Tigbauan, Iloilo 21 July 1995.

A drug by any other source heals as good ...



by A. SURTIDA



Better life through aquaculture