

# BIOPROSPECTING IN A POST-CASTRO CUBA

Larry Daley

The intent is—in post-Castro Cuba—to establish bio-prospecting laboratories in the rain-forests of eastern Cuba and fund them through a combination of commercial, international agency and U.S. based federal grant funding for visiting researchers. The task of these laboratories will be to seek pharmacologically, medically, and agriculturally useful biochemicals among the exceptionally diverse plant, and fungal flora, and the fauna of Cuba.

What is proposed here differs from anything the present government does. This is because this project is designed to be run by free people, independent researchers, and funded by a combination of private pharmaceutical and agro-business sources, competitively funded U.S. granting agencies and private foundations.

The expected benefits include those associated with rain forest preservation and restoration, cleaner water, preservation of biological diversity, reduction of erosion. The political stabilization of the area and increased welfare of the local inhabitants is also an expected outcome. The areas designated for this use are the mountain heights between the Guamá and the Bayamo valleys which are biologically very diverse and steeped with Cuban history and deserve to be clean and free and forested again (Enamorado, 1917).

## FUNDING

This should not be thought of as a government funded project. A free and democratic Cuba will have enough demands on public funding. Thus, contemplated sources of bioprospecting funding include:

## Private Companies

Bioprospecting can be a source of great profits as the history of Syntex corporation has shown. In varying levels of detail, some authors have discussed the returns from the bioprospecting (Katzman and William, 1990; Lesser and Krattinger; 1994; Hodson *et al.*, 1995 Moran, 1996) and have come up with positive estimates. One paper (Simpson, 1997) believes it would be negative. However, while the authors of the above papers are certainly interested parties, Simpson's analyses seems to also to be partisan where ethical and ecological considerations are given greater weight than potential profits. In my view Simpson, although he does make some convincing points, underestimates the efficiencies of modern screening technologies. He seems less aware of both biochemical diversity which he assumes to be more repetitive than the vast mass of literature on "natural products" plant biochemicals would suggest. It would seem that further and more formal economic studies should be made using whatever real life data is available; Lesser and Krattiger (1994) have made a good start.

## International Funding

Another source of economic returns is international agency funding to compensate for such things as fossil fuel burning in the more highly developed countries (e.g. Gass and von Loesch, 1996; Putterman, 1994). The situation of Cuba adds other political and environmental recovery reasons to supplement fund (Díaz-Briquets, 1996). In my view one of the most urgent reasons to seek to retain Cuba's forests, aside from the erosion and diminishing the peak run offs (Díaz-Briquets, 1996), is the potential contribution to political stability of remote areas (see

below). This political consideration may also attract funding.

### Visiting Scientists

A third source of funding is the renting of facilities to visiting scientists. Contact has been already made with scientists who in their research visit the areas selected. It is common for many U.S. university-faculty to seek and obtain this kind of funding for sabbaticals and summer terms. Research facilities such as Cold Springs Harbor in the United States and “La Selva” in Costa Rica supplement their funding in this way.

### Protection of Migratory Birds

There is U.S. funding support for the protection of migratory birds and the protection of non-migratory species. This area may be one of the last areas on earth where a significant and well-loved bird, the ivory-billed woodpecker, survives. This funding would be directed at the maintenance of shade coffee, which makes an excellent migratory bird habitat (Rice *et al.*, 1996). The funding is to compensate for the loss of production associated with the shade—as opposed to the sun coffee production—method. The area in Cuba under consideration has old coffee groves. These groves could be maintained in this use with this funding support, until the coffee bushes age and become less productive, and trees that provide the shade grow very large and the area starts to return to forest.

### POLITICAL REASONS TO RESTORE THE RAIN FOREST

In the past it has proven politically destabilizing to permit the destruction of forest by allowing slash and burn agriculture. This leads not only to the destruction of the forest but also to heart-breaking human misery. Having seen this first-hand it is hard to think of this situation dispassionately. Slash and burn agriculture as done in the Sierra Maestra was labor intensive and the ambition to cut large swaths of forest and keep the crops weed-free required much work, thus promoting excessively large family size.

The area was remote from most schools, and from the law. To feed their large families these children frequently just worked their parents holdings and did

not attend school; thus as they grew up these children only knew slash and burn agriculture. Repeating the cycling these children at a very early age also started families. This situation rapidly generated large numbers of illiterate, easily influenced, poor and desperate people, often called Montunos (people of the forest and the mountain), unaccustomed the rule of law. As families grew young men and women in search of their own lives, and independence from their families were always ready to seek more forest to cut. In these circumstances all who owned rain forest and wished to hold their land had to cut forest or it would soon be filled with squatters. It was a constant struggle just to maintain trees along the water courses. Erosion and flooding became more prevalent.

Then came the revolution of 1956-1959. In the morass of things that followed, Sorí Marín—defender of the Montunos—and possibly some of the Montunos of the area were executed. Life in the mountains grew even harsher, and much land in the mountains was abandoned (Díaz-Briquets, 1996).

In the present phase of transition, there is a lack of fuel, people in cities like Bayamo have no way except to use firewood to cook. I understand that this is again generating pressure on the forests, especially since in misguided attempts to “improve” and centralize agriculture there are now few trees on the plains (Díaz-Briquets, 1996). Even the live fence post trees (*Gliricidia spp.*), which would normally provide a considerable amount of cuttings for replanting or firewood (64 Kg of green-wood /year/tree in Sri Lanka, Allen and Allen, 1981 pp. 300-302) are gone. Such live fences must be replanted to spare the forest.

### CUBAN RAIN FORESTS AS A SOURCE OF PHARMACEUTICALS

Rain forests are increasingly important sources of valuable pharmaceuticals and other bioactive products, and each different rainforest is a source for different bioactive compounds. In the rain forest, water and temperature do not limit growth; here interaction between species determines survival. The plants, animals, and fungi found in these areas are in relentless competition, species form and break alliances for defense, and to attack or exclude other species. Pathogens rapidly adapt, attacking any specie that

## GLOSSARY OF TERMS AND CONCEPTS

**Biochemical diversity:** The root of diversity is the complexity of life's biochemistry (Cagri and Younes, 1996). Each species of life be it plant, animal, fungi, and microorganism shares basic biochemical functions of DNA, RNA and enzymes (e.g. Taiz and Zeiger, 1991; Voet and Voet, 1995). Simple observation tells us that these basic biochemical functions give different results. One readily distinguishes between a fly and a human, poison ivy and a palm tree, a cow and a pig.

Yet, it is not always possible to tell life forms apart so readily. Take for instance edible mushrooms and deadly *Amanita phalloides*, the death angel mushroom (Klein, 1979 p. 173). Biochemicals—in this case the complex cyclopeptides found in this deadly fungus—make a mayor difference between these species. An extract containing these cyclopeptides, and a very supportive mother, allowed Nero to become Emperor of Rome. Even today, one thousand nine hundred and forty three years after Nero, some wild mushroom pickers, do not always make the distinction between species of mushrooms. These pickers dying regrets very forcefully make the point that biochemical differences between species do matter.

Even closely related species have different biochemistry, a classical case is the massive tristeza disease disaster of citrus crops which occurred about forty years ago South America. This financial and agricultural disaster was a direct result of the mandated use of the sour-orange rootstock instead of the tristeza tolerant root stock such as rough lemon, sweet orange (Pratt, 1958). The biochemistry of the sour orange rootstock is such that the rootstock does not thrive when infected with tristeza. The infected rootstock does not provide sufficient water and minerals to the upper part—the grafted sweet orange bearing part—of the tree. Thus the tree sickens, saddens, and dies.

**Bioprospecting:** Bioprospecting is the search among the diversity of life's millions organisms—and the many millions if not billions of biological compounds found in these organism—for biochemicals of use to humanity especially for pharmaceutical and agricultural uses (Rouhl, 1997). Bioprospecting is—like prospecting for minerals—a game of numbers. A way to measure, to assay, the desired activity called a screen (see below) is set up, and thousands of relatively crude samples—each containing many biochemicals—are processed through the screen to find one or more that works. The more species one examines, the greater the chance is that one will find the desired activity. Some times each sample is fractionated, usually by some chromatographic technology, into different groups of biochemicals before this assay this screen is performed.

**Diversity:** Diversity is a much bandied about word which in the common use and in the press. Is commonly given a fuzzy meaning evoking images of verdant beauty and forests and falling rain with dedicated, usually hirsute, almost mad, ecologists struggling to protect this treasure against evil despoilers of nature. Somehow, per-

haps because many ecological activists talk little about biochemistry and pharmacology the word diversity has become a mantra, a word of sacred content, pregnant with symbolism, but seemingly without precise meaning. However, there is hard science, much international political maneuvering, great commercial value and interest behind all this talk of diversity (Dudenhoefer, 1997; Cagri and Younes, 1996; Gass and von Loesch, 1996; Hodson, *et al.*, 1995; Katzman and Cale, 1990; Lesser and Krattinger, 1994; von Loesch, 1996; Moran, 1996; Putterman, 1994).

**Diversity within species:** Diversity also exists within species. We all know the commercially significant difference between a Leghorn and Barred Plymouth Rock chicken or between a green Granny Smith and Red Delicious apple. Here the colors tell us that the different feathers or the different colored peels are biochemically different. These intra-specific differences can have tremendous commercial significance in such circumstances as disease or pest significance. For instance, presence of *Septorium* resistance in wheat strains (Kronstad, personal discussions, 1996) is critical to the profitability of crop in the Willamette Valley.

**Economic consequences of diversity:** Ignoring these difference, this diversity of plant materials, has led to massive crop failures. Thus, diversity and its ownership is matter of great concern for crop breeders and agricultural development agencies (Gass and van Loesch, 1996; van Loesch, 1996). Diversity is based upon variability in biochemistry and that variability in biochemistry extends below the species level to distinguish the individual plant or clone.

**Germplasm:** Germplasm refers to the living organisms that carry the diversity of life. Germplasm is defined as “the genetic donors: DNA sequence information, DNA, RNA, and protein sequences, cells, seeds, propagules, clones, plants organisms, etc., which are available or potential sources of variation in genetic composition” (Feng, *et al.*, 1994). The biochemistry of each individual plant varies not only with their genetic composition germplasm, but with the season, and the part of the plant: leaf, seed root etc, which have different biochemical components. (See discussion of site for screening below.)

**Pharmaceutical interests:** For a plant scientist the preservation of plant and animal germplasm is very significant. However for human medicine, as diseases constantly emerge, change, and acquire resistance to older treatments, it is essential to find new biochemicals that can act as new drugs, and antibiotics, etc. For these reasons bioprospecting is an active field; and there is a continual search, not only among the plant and animal kingdoms, but also among the bacteria and the fungi for new drugs and antibiotics. Scientists seek biochemicals in living organisms for several reasons: (1) there is vast number of biochemicals in living organisms; (2) there is a tradition of finding pharmaceuticals in this way; (3) many bio-

chemicals have very complex chemical structures and chirality that are either too difficult to synthesize or simply cannot be made in the laboratory; and (4) the synthesis of a biochemical in a living organisms—as opposed to making it in the laboratory—mean that such biochemicals generally are not harmful to the cells in which they live (Gerwick, personal communication, 1996).

**Rain forest:** A rain forest is a heavily forested area of high rain fall where species diversity is high, trees grow tall and then branch out at different heights generating two or three separate canopies. Fallen trees decompose and rot to support a large number of other organisms. In family legends, I was told as a child that large white grubs were found inside these fallen giants. Grubs that last century the Cuban Insurgents, the Mambises, ate when there was nothing else to eat. There are large numbers of species of trees, lower story and epiphytic vegetation, and associated fungi, microorganisms and fauna. The value of the rain forest is in its biochemical diversity. “The immense biological diversity of tropical forests is difficult to comprehend. For example, ten selected 10-hectare plots in Borneo contain 700 species of trees and 1 hectare of tropical Peru contained 300 tree species. By comparison, 700 species of trees occur in all of North America” (Skole and Tucker, 1993).

**Screening** Today the screening process is highly automated. Automation is very necessary because one could expect a positive result from about 1/12,000 samples (e.g. Lesser and Krattinger, 1994). This new technology with its great sensitivity and through-put discovers new biochemicals, with new agricultural, biological and pharmacological activities at a much faster rate than ever before. Through use of anecdotal, traditional folk medicine, information the proportion of active biochemicals to inactive biochemicals can be enhanced considerably (Moran, 1996). Such information is available for a good number of Caribbean plants (Robineau, 1991).

Still each screen usually only determines one or few activities, thus for each activity it is usually necessary to set up a new screen. Since the array of biological materials screened for one purpose will almost certainly contain many other activities, the same array of biological materials can, and should, be run through other screens. This is a game of numbers and endless research.

**Site:** Today much of the screening research is done in separate academic and governmental centers far from the source of the materials. Although one way to make the screening process more effective is to establish on site centers of investigation (Putterman, 1994). Such on site laboratory centers might help reduce scientific unemployment, were post-Castro Cuba to follow the German Renunciation model and decrease the number of scientists staffing at government laboratories.

**Synthetic genes:** A synthetic gene is one designed by man and made on a machine: on a DNA synthesizer. Synthetic genes, although used for basic experiments, are seldom if ever used in bioengineering, instead genes are taken from a living system. To be useful in bioengineering a DNA sequence must efficiently guide the generation

of an RNA sequence. That RNA sequence must efficiently guide the synthesis of a protein; and the protein, the enzyme, made in this process must work better than the natural enzyme.

Synthetic genes have difficulties (Chen, personal communication, 1997) because the sequences designed by man rarely function as well as evolved genes found in living organisms. Natural genes have been honed by evolution over many millions of years. For instance to my knowledge, despite massive research effort, no synthetic gene for ribulose bis-phosphate carboxylase (the very critical enzyme of carbon fixation and the enzyme on which all life on earth depends) has proven to be more efficient than the natural enzymes. Difficulties with synthetic genes are that they often: (1) yield proteins alien to the cell and thus these proteins are broken down by cell proteases; (2) generate an insoluble protein which precipitates in the cell, and does not function; (3) generate an enzyme or structural protein that does not fold to the correct conformation and not thus have the appropriate catalytic action; (4) generate synthetic RNA codes from the introduced DNA that are not compatible with host's protein synthesis apparatus and little if any of the new protein will be made; and (5) do not work as well as very efficient natural genes.

Thus to date synthetic genes are a laboratory tool, not a way to bioengineer new and better living beings. On the other hand a DNA sequence from nature, say from a Cuban rain forest tree, will have evolved to maximum efficiency for its function in that plant.

**Transformant bioengineering technology:** Not so long ago plant breeders were limited to diversity within the same species or species closely related enough to interbreed. Then, if a crop had a new disease and there was no related plant with a resistant gene, “it was simply too bad.” Farmers had to live with the disease. For example Gross Michel variety of bananas are very hard to breed (Tempany and Grist, 1958, p. 172). Long ago, Panama, Cuba and many other countries' banana crops were attacked by “El Mal de Panama” *Fusarium oxysporium f. cubensis* (*Fusarium cubense* E.F. Smith) Snyder and Hansen (Cook, 1939, pp. 245-250). Cuba lost a major crop. Eventually with much difficulty and expense resistant varieties were bred using traditional methods and genes from the Cavendish variety (Cook, 1939, p. 250; Tempany and Grist, 1958, p. 172.).

Now that bananas can be transformed, bioengineered, even to produce vaccines (Strobel, 1995, personal communication), introduction of a pathogen resistant gene is not as difficult. Now a gene can be taken—not only from one plant to a related plant—but also genes can also be moved to crop plants from unrelated plants that would never cross, even from animals and from fungi. This is what makes tropical and semitropical forests so important. These forests are full of plant diseases and insects. To survive under these conditions these plants have had to evolve resistance to them. This resistance, almost always, involves biochemicals.

becomes too numerous. Species diversity is the rule. New species, with new ways of survival, arise. Older species adapt and fight back. Much of the competition and many alliances are carried out using bioactive biochemicals.

The intense biochemical competition between host, pathogen, parasite and herbivores produces many bioactive products. To be most effective, a bioactive product should attack an important biochemical pathway of pest, pathogen, etc. without harming the host species. Many biochemical pathways are general and are common throughout life. Thus, other organisms can produce bioactive products harmless to man, but active against man's pathogens; when such products are found, they have pharmaceutical potential. One of the more famous bioactive products obtained from forest is taxol (Baskin *et al.*, 1994; Stierle, *et al.*, 1993), a compound—extracted from northern forest trees—used for cancer treatment. More pertinent to Cuba, for example, are the trees of the Annonacea family. These trees and their fruit have a number of useful and potentially useful bioactive materials such as parviflorin which has remarkably selective cytotoxicity against certain human solid tumor cell lines (Hoye and Zhixiong, 1996). Many other examples exist: e.g. thionin proteins, which are found in tropical as well as temperate climate plants. Thionins were once thought of as merely interesting redox proteins. Now thionins can be used to bioengineer fungi and bacteria resistant plants (Carmona *et al.*, 1993; Daley and Theriot, 1987; Molina, *et al.*, 1993). New ways of purification, new automated screening assays, and increasingly efficient biotechnological production methods have made the search for bioactive products much more economically viable.

#### **Access to Rain Forest Bioactive Products**

Seeking the bioactive products of the rain forest is not easy. Collections of seasonal products is difficult because climatic and heat conditions frequently make long stays difficult. Then there are difficulties with the local legal and business environments and legal barriers against export of germplasm. This paper explores a plan to avoid some of these difficulties by taking advantage of the opportunity to plan now for

access to the rain forest of Cuba when Castro falls (Díaz-Briquets, 1996).

#### **Influence of Geology and Isolation on Genetic Diversity**

Genetic diversity of flora and fauna (germplasm) and regional divergence of germplasm determine each rain forest's products. More prolonged geological isolation, and greater diversity of habitats favor more unique arrays of component germplasm (Borhidi, 1991; Leon and Alain, 1946-1953, 1974; Schultes and Raffauf, 1990; Skole and Ticker, 1993; Terborg, 1992; Victorin and Leon, 1944). This enhances the potential of a particular rain forest to harbor distinctly different kinds of commercially valuable products. Cuba is such a place (Borhidi, 1991).

About 38 million years ago, less than 100 miles south of what is now the United States, great geological changes occurred (MacPhee and Iturralde-Vinent, 1994). The Greater Antilles Ridge arose from the sea, and in the next twenty or so million years, this ridge first joined then separated from South America, forming the Greater and Lesser Antilles. The westernmost islands that would become Cuba were separated from the rest of this complex by the rejuvenation of the Oriental Fault of which the Deep of Bartlett (also known as the Cayman Trench) forms a part. After this, with the exception of air and avian borne seed, the ancient South American Oligocene plant and terrestrial animal germplasm speciated and diverged in isolation to become unique Cuban species. At this time, large mammals such as giant rodents and enormous ground sloths roamed the coalescing islands that form Cuba today (MacPhee and Iturralde-Vinent, 1994). Arriving much later in Cuba than in other areas of the Americas, Paleo-Indians eventually wiped out this megafauna. However, some believe that even the ground sloth survived in neighboring Haiti until the time of William the Conqueror or perhaps later (Walker *et al.*, 1964). While the megafauna became extinct, the vegetation and many smaller animals, including some mammals survived, and could still be living in the rain forests of Cuba near the selected site (Walker, *et al.*, 1964; Barbor, 1944).

### Human Health and Living Conditions in the Eastern Cuban Rain Forest

In most of the world the surviving rain forests, especially those that are most diverse, are frequently not easily accessible, and are unhealthy and dangerous, which make these areas more expensive to survey for bioactive products. Cuba's rain forests are free from poisonous snakes. Reservoirs of yellow fever and malaria were wiped out after the United States helped liberate Cuba from the Spanish (1898) and controlled the infected mosquitoes that spread these diseases. The general area is very scenic, relatively cool and healthy, and readily accessible from Jamaica, the Cayman Islands and various cities, ports and towns on the eastern Cuban plains. There should be little difficulty recruiting appropriate staff.

### Rain Forest Regeneration

It is a commonly held misconception that all rain forests, such as described by Skole and Tucker (1993) for Amazonia, once cut do not re-grow because the soils degenerate. Personal experience shows that does not occur as intensely in the limestone and ancient igneous rock derived 'laja' soils of the mountains of eastern Cuba. Cuban rain forest is resilient. As long as 'cayos' of rain forest persist, fungi, primitive vascular plants, tree ferns, etc. regenerate from wind born spores. Angiosperm seeds are frequently dispersed by birds, wind and water from undisturbed sections of the forest. Other angiosperms are spread on the coats or in the droppings of cattle, pigs and horses that replace, in this respect, the extinct megafauna. Today in Cuba, the guásima (*Guazuma ulmifolia* Miller.) or bastard cedar or West Indian elm tree (Fors, 1956) still grows in Cuban pastures. While once dispersed by the extinct megafauna (Mabberley, 1993, p. 255), this tree is now dispersed by cattle that eat the seed and pass the seed in their droppings. Underground roots spread from adjacent undisturbed land or survive for years in cultivated fields; for it is a constant struggle to maintain pastures of trees and crop fields free of lianas, to stop the formation of the "bejuquero".. Thus, if left undisturbed, tropical rain forests can rapidly re-expand their range. For instance, the valuable Cuban fine wooded Leguminosae *Lysiloma latisiliqua* (sabicú) grows five feet in the first year (Fors, 1956; Jiménez

Aguilla, *et al.*, 1991). Recolonialization is even faster for tree species such as yagrumas (*Cecropia peltata* and *Didymopanax morototoni*), which yield poor lumber, yet have bioactive potential because of their complex association with ant colonies (Copeland and Moiseff, 1997). However, a word of caution, as Gómez-Pompa points out that eco-system recovery, may mask diversity loss (Rice *et al.*, 1997, p. 2.) so there is not that much time to lose

### Historical Events that Promoted Survival of Cuban Rain Forest

Growing in very complex and intermingled habitats on cave riddled limestone and igneous based mountains, rain forests still exists in areas of eastern Cuba. Some of this rain forest was cut back for coffee plantations in the early and middle 1800s, mainly by French immigrants displaced from Haiti. However, this activity ceased and the rain forest again closed in on these holdings during the prolonged struggle of the Cubans to free themselves from Spain (Enamorado, 1917). These wars were of considerable intensity and duration. By the end of the nineteenth century, after freedom from Spain, Cuba's small population was reduced by at least one third. Between the turn of the century and the 1950s, the expanding population gradually pushed back the rain forest. The rain forests range was to a few small areas in the middle of the island and somewhat larger areas of the old eastern province of Oriente (Marrero, 1955).

The expansion of farming into this area was halted by the revolts (1957-1959) against Batista's dictatorship. Then Castro's government converted large amounts of this area to military zones, and displaced the traditionally rebellious montuno, mountain population, to exile or towns and collective farms on the plains. The rain forest area, a traditional refuge of disaffected populations for five centuries, is now laced with military roads constructed first by Batista and then greatly expanded by Castro, despite continued landslides, and only sporadically populated between military garrisons.

### THE COMING CHANGE IN CUBAN BUSINESS ENVIRONMENT

Despite the present Cuban government's desperate attempt to survive, its power is slipping away and a

much more open and democratic government can soon be expected to replace it. The new Cuban government will need to rely heavily on the very successful Cuban exile business community of the United States to redevelop the economy. Thus, a free Cuba can be expected to have a business environment much more like the United States, than other countries which have rain forest resources, but also insular business methods less favorable to U.S. investment and licensing procedures.

### **The Effects of This Change on Cuban Rain Forests**

As the Castro government loses its tight control over the population, the mountain land will again be open to development (Díaz-Briquets, 1996). Additional pressures on the rain forest will arise because this is also a mineral rich area with proven deposits of manganese, copper, silver and gold (e.g. Simons and Straczek, 1958; Oro, 1992 and personal memories). It is necessary to plan to protect the rain forests now. If plans are not in place, there will be little time to make them when Castro's fall triggers a rush to repopulate the area and clear the rain forests for agriculture.

### **Satellite Imagery**

This is our first step. At present, satellite imagery is the only certain way to access information on the Cuban rain forests. Ground and air access to Cuba's rain forests is extremely limited. It is necessary for our purposes to determine how much of the Cuban

rain forest remains, and if and where the rain forest has re-expanded. The Cuban government's data and concern for rain forest survival are not considered reliable. Castro's government has built strategic military roads, strong points and dams, with concurrent damage to ecology (Díaz-Briquets, 1997). Although we do not have on ground or over flight information, and no U.S. company representative can go into the area, commercial satellite data can readily provide information on the extent and health of the rain forest using standard techniques.

The plan is to use available satellite image data to survey the present extent of the rain forest (Cohen and Spies, 1992). Locations have already been found using United States Board on Geographic Names 1963 data and computerized versions of this same data provided by the Defense Mapping Agency. Only when this data is known, can plans be developed to contact and reach exploration and preservation agreements with those holding title to the critical areas before Castro falls. This will allow the new Cuban government to stay the final destruction of its unique rain forests (Díaz-Briquets, 1996, 1997), while legitimizing the rights of private industry to seek and utilize the bioactive compounds from these areas. Thus, our first step is to map, by remote sensing, the critical, most germplasm rich, potential sources of pharmaceuticals and bioactive substances in the eastern Cuban rain forest.

## **ANNOTATED BIBLIOGRAPHY**

Allen, O.N. and Allen, E.K. 1981. *The leguminosae: A source book of characteristics, uses and nodulation*. Madison: University of Wisconsin Press, 812 pp. This is used as an example of reference text illustrating both the botany and the bioactive products of just one family of tropical plants, many of them rain forest trees.

Barbor, T. 1944. "The solenodons of Cuba." Proceedings of the New England Zoological Club

23, 1-8. Locates the almiquí in old Oriente Province, near Bayamo among other places.

Baskin, T.I., Wilson, J.E., Cork, A., and Williamson, R.E. 1994. "Morphology and microtubule organization in *Arabidopsis* roots exposed to oryzalin or taxol." *Plant Cell Physiol.* 35, 935-942. This paper illustrates the way bioactive products affect all life. Taxol, a bioactive plant and fungal product, is a useful treatment for cancer in humans.

- Borhidi, A. 1991. *Phytogeography and vegetation ecology of Cuba*. Budapest: Akademiai Kiado, 857 pp. (Translation of a Hungarian flora of Cuba.)
- Carmona, M.J., Molina, A., Fernández, J.A., López-Fando, J.J., and García-Olmedo, F. 1993. "Expression of the a-thionin gene from barley in tobacco confers resistance to bacterial pathogens." *Plant J.* 3, 457-462. Example of thionin action and bioengineering. Transfer of *Pseudomonas* resistance from barley to transgenic tobacco.
- Castri, F. di and Younes, T. (eds). 1996. *Biodiversity, science and development*. Wallingford, England: CAB International.
- Cohen, W.B. and Spies, T.A. 1992. "Estimating structural attributes of Douglas-fir/western hemlock forest stands from Landsat and SPOT imagery." *Remote Sens. Environ.* 41, 1-17. This is an example of the use of satellite imagery to determine forest stand structure and "wetness" of forest.
- Copeland, J. and Moiseff. 1997. "Ants on *Cecropia* in Hawaii." *Biotropica* 29,128-132. Although this paper deals with non-native species in Hawaii, where neither the ants nor its host trees are native, there is a good review of this complex and potentially useful plant-insect relationship.
- Cook, M.T. (translated by José L. Otero). 1939. *Enfermedades de las Plantas Económicas de Las Antillas*. San Juan: University of Puerto Rico Monograph, Series 2. Number 4.
- Daley, L.S. and Theriot, L.J. 1987. "Proteins-similar to purothionin from tomato (*Lycopersicon esculenta*), mango (*Mangifera indica*), papaya (*Carica papaya*) and walnut (*Juglans regia*). Purification, protein redox activity, and effect upon proteolytic activity." *J. Agric. Food Chem.* 35, 680-687. First demonstration of thionins in tropical species. This work continues successfully in more applied, but still unpublished form in laboratory of the author.
- Díaz-Briquets, S. 1996. "Forest policies of Cuba's socialist government: An appraisal." *Cuba in Transition—Volume 6*, 425-437.
- Díaz-Briquets, S. 1997. *The Environmental Legacy of Socialism in Cuba*. Manuscript in submittance.
- Dudenhoefer, D. 1997. "Costa Rica conference focuses on nexus between business and biodiversity conservation." *Diversity* 13, 7-8.
- Enamorado, C. 1917. *Tiempos Heróicos: Persecución*. La Habana: Imprenta y Papelería de Rambla, Bouza y Cia., 255 pp. Prize winning book, written by a general of the Cuban wars against Spain, a diplomat and scholar who, in later years was very interest in plant germplasm. The book is placed in, and describes in detail, the extent of the rain forests of the area in the middle and late nineteenth century and provides firsthand details on Cuba's eastern rain forests' vegetation and rivers not available elsewhere.
- Feng, W., Ning, L. Daley, L., Moreno, Y., Azarenko, A. and Criddle, R. S. 1994. "Determination of effective temperature minima for CAM carboxylation in diverse plants by scanning microcalorimetry." *Plant Physiology and Biochemistry* 32, 319-330.
- Fors, A. J. 1956. *Maderas Cubanas*. La Habana: Ministerio de Agricultura, 162 pp. This book describes many of the rain forest trees' growth habits, etc. in considerable detail. The author also wrote the present Cuban government forestry manual. Fors, A. J. 1966. *Manual de Silvicultura*. La Habana: Publicaciones INRA, Havana, 237 pp.
- Gass, T. and Loesch, H. von. 1995. "Genetic resources targeted as a priority for new CGIAR thrust in Eastern Europe and NIS states." *Diversity* 12(4), 3.
- Hodson, T.J., Englander, F., and O'Keefe, Hsu. 1995. "Rain forest preservation, markets, and medicinal plants: Issues of property rights and present value." *Conservation Biology* 9, 1319-1321.
- Hoye, T. and Zhixiong, Y. 1996. "Highly efficient synthesis of the potent antitumor annonaceous acetogenin (+)-parviflorin." *J. Amer. Chem. Soc.* 118, 1801-1802. The first paragraph of this pa-

per reads: "The annonaceous acetogenins are a rapidly growing class of natural products that have received considerable attention. Many members (of this plant family) possess a variety of biological effects including potent cytotoxic, antitumor, and pesticide activities. parviflorin, a relatively rare C<sub>35</sub> bis THF acetogenin, was isolated by McLaughlin et al. both from *Asimina parviflora* Duanl and from *Annona bullata* Rich. Parviflorin showed remarkable selectivity in its cytotoxicity against certain human solid tumor cell lines."

Jiménez Aguilla, M., Calzadilla Zaldívar, E., Renda Sayous, A., Sánchez Rodón, J., Torres Torres, J., and Casate Tenrero, C. 1991. "Los sistemas agroforestales: Alternativa para manejo integral de los suelos montañosos de Cuba," *10th Proc. World Forestry Congress* 3, 28-34. These authors report growth of replanted native trees in prepared terraces in igneous based soils on the foot hills below (less than 700 feet elevation) the rain forests of eastern Cuba. For instance, the rapid growing, highly prized, native rain forest timber source *Lysiloma latisiliqua* (sabicú, jigüey) is reported to reach a mean height of almost 12 feet in 27 months.

Jiménez Arrellanes, A., Mata, R., Lotina-Henssen, B., Anaya Lang, A.L., and Velasco Ibarra, L. 1996. "Phytogrowth-inhibitory compounds from *Malmea depressa* (syn. *Gutteria leiophylla*)." *J. Nat. Prod.* 59, 202-204. This paper is used as an example of studies that could be done in Cuba, since the species studied is related to naturally occurring Cuban species *Gutteria Blainii* and *Gutteria Moralesii*.

Katzman, M.T. and Cale, W.G. Jr. 1990. "Tropical forest preservation using economic incentives." *Bioscience* 40, 827-832.

Klein, R.M. 1979. *The Green World*. New York: Harper and Row.

León, H. and Alain, H. 1946-1953, 1974. *Flora de Cuba*. Koenigstein: Otto Koeltz Science Publishers. Part of the classic life work on Cuban flora

(description of plants) of the monk Hermano León (see also Victorín and León below). Since these authors belong to a religious order, their first name is given as Hermano which translates to Brother in English and Frere in French, thus initials, are B., F. or H., depending on the language of the citation.

Lesser, W.H. and Krattiger, A. F. 1994. "The complexities of negotiating terms for germplasm collection." *Diversity* 10, 6-10.

Loesch, H. von. 1996. "World Bank official warns of future 'Scientific Apartheid.'" *Diversity* 12(4), 5.

MacPhee, R.D.E. and Iturralde-Vinent, M.A. 1994. "First tertiary land mammal from Greater Antilles: an early Miocene sloth (*Xenarthra*. *Megalonychidae*) from Cuba." *American Museum Novitates*, number 3094, 1-13. Although the dating of this find is subject to scientific discussion, the description of the geological development of the Antilles, by virtue of the two authors' contacts in present day Cuba, is very useful for the purposes described here.

Marrero, L. 1955. *Geografía de Cuba*. La Habana: Alfa. 736 pp. This book contains a large number of aerial photographs of the rain forests of eastern Cuba as they existed in the late 1940s and 1950s, and thus is very useful for comparisons with data on present extent of rain forest to be obtained in this proposed project. In addition, very complete rainfall and some soil information is provided for all areas including the rain forests.

Mabberley, D.J. *The plant-book*. Cambridge, England: Cambridge University Press.

Moran, K. 1996. "Compensating forest-dwelling communities for drug discovery: The work of the Healing Forest Conservancy." *Unasilva* 47, 40-46.

Molina, A., et al. 1993. "Inhibition of bacterial and fungal plant pathogens by thionins of types I and II." *Plant Science* 92, 169-177. Example of range of activity of thionin proteins.

- Oro, J.R. 1992. *The poisoning of paradise*. Miami: Endowment for Cuban American Studies.
- Pratt, R.M. 1958. *Florida Guide to Citrus Insects, Diseases and Nutritional Disorders*. Gainesville, Florida: Agricultural Experiment Station.
- Putterman, D.M. 1994. "Trade and the biodiversity convention." *Nature* 371, 553-554.
- Rice, R.A., Harris, A.M., and McLean, J. 1996. *Proceedings 1st Sustainable Coffee Congress*. Washington: Smithsonian Migratory Bird Center, National Zoological Park. A compendium of the relationship between different types of coffee growing practices and bird habitat, with rain forest recovery aspect included.
- Robineau, Lionel. 1991. *Towards a Caribbean Pharmacopoeia: Scientific Research and Popular Uses of Medicinal Plants in the Caribbean*. Santo Domingo, Dominican Republic and Universidad Nacional Autonoma de Honduras: Enda-Caribe. This is a very catholic source of data varying from the traditional medicine traditions to scientifically reviewed publications.
- Rouhi, M. 1997. "Seeking drugs in natural products." *Chemical & Engineering News* 75(14) (April 7, 1997), 14-29. An interesting article that, among other things, discusses the changes in bioprospecting practices in recent years, a number of successful and promising enterprises in this field, and the effectiveness of different biosprospecting practices
- Schultes, R. E. and Raffauf, R.F. 1990. *The healing forest. Medicinal and toxic plants of Northwest Amazonia*. Portland, Oregon: Dioscorides Press. Richard Evans Schultes is Jeffrey Professor of Biology and Director of the Botanical Museum of Harvard University and a very well known medicinal plant explorers. This book illustrates the great number of bioactive materials found in rain forests. One should keep in mind that, although some species and genera overlap, the flora of Cuba is different from that of Amazonia. Thus Cuba's flora with its large number of endogenous species is another rich source of bioactive compounds.
- Simons, F.S. and Straczek, J.A. 1958. *Geology of manganese deposits in Cuba*. U.S. Geological Survey Bulletin 1057. This bulletin contains maps of the site area.
- Simpson, R.D. 1997. "Biodiversity prospecting." *Resources* 126, 12-15
- Skole, D. and Tucker, C. 1993. "Tropical deforestation and habitat fragmentation in the Amazon: Satellite data from 1978 to 1988." *Science* 260, 1905-1910. This paper describes a similar application of remote sensing technology to what we propose.
- Stierle, A., Strobel, G. and Stierle D. 1993. "Taxol and taxane production by *Taxomyces andreanae* an endophytic fungus of pacific yew." *Science* 260, 214-216. The first report of the finding of the cancer treatment drug, taxol, in an endophytic fungus. This reference shows bioactive compounds can be found in complex associations of different organisms and documents the established competence of one of the author's associates to search for bioactive compounds.
- Taiz, L. and Zeiger, E. 1991. *Plant Physiology*. Redwood City, California: Benjamin/Cummings.
- Tempany, H. and Grist, D. H. 1958. *An introduction to tropical agriculture*. London: Longmans, Green and Co. This old but still useful book gives an idea of how difficult breeding of some tropical crops could be before biotransformation greatly expanded the sources of genetic diversity available to breed each crop plant species.
- Terborgh, J. 1992. *Diversity and the tropical rain forest*. New York: Scientific American Library. A less specialized approach to the general aspects of rain forest diversity and value. The lush illustrations and quality of this book are a reflection of the great popular interest in rain forest conservation.
- United States Board on Geographic Names. 1963. *Cuba*, 2nd edition. Washington: Office of Geog-

raphy, Department of the Interior. 619 pp. Locates many of the smaller rivers and population centers in great detail, giving latitude and longitude, allowing precise localization for SPOT imagery. An updated version is available on CD disks from the Defense Mapping Agency.

Victorín, F.M. and León, F. 1944. *Itinéraires botaniques dans l'île de Cuba*. Montreal: Botanical Institute of the University of Montreal. 410 pp. A classic reference on Cuban vegetation.

Voet, D. and Voet, J. G. 1995. *Biochemistry*, 2<sup>nd</sup> edition. New York: John Wiley & Sons, Inc.

Walker, E.P., Warnik, F., Lange, K.I., Uible, H.E., Hamlet, S.E., Davis, M.A., and Wright, P.F. 1964. *Mammals of the World*. Baltimore: The John Hopkins University Press, Baltimore. In volume 1, p. 483, describes ground sloth remains found in Hispaniola and Puerto Rico associated with human pottery, bones of man, and domestic pig. Pp. 104-105 of the same volume describe the almiquí (*Solenodon cubanus*). Volume 2, pp. 1033-1035 describe and illustrate *Capromys spp.* the jutías.