THE PLANT KINGDOM AS A SOURCE OF NEW MEDICINES

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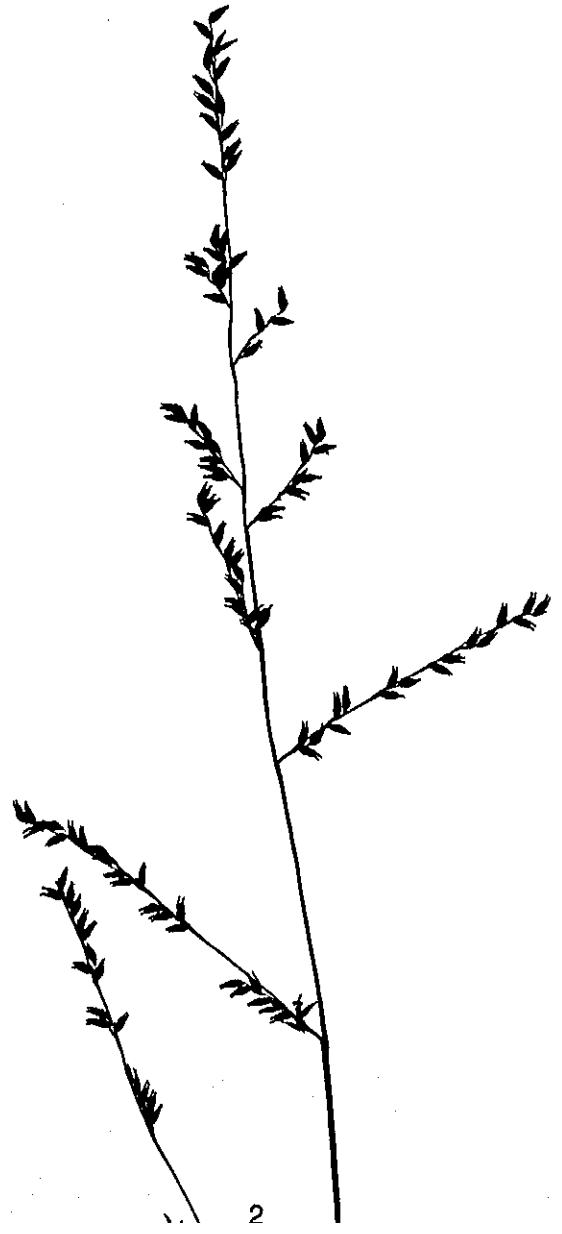
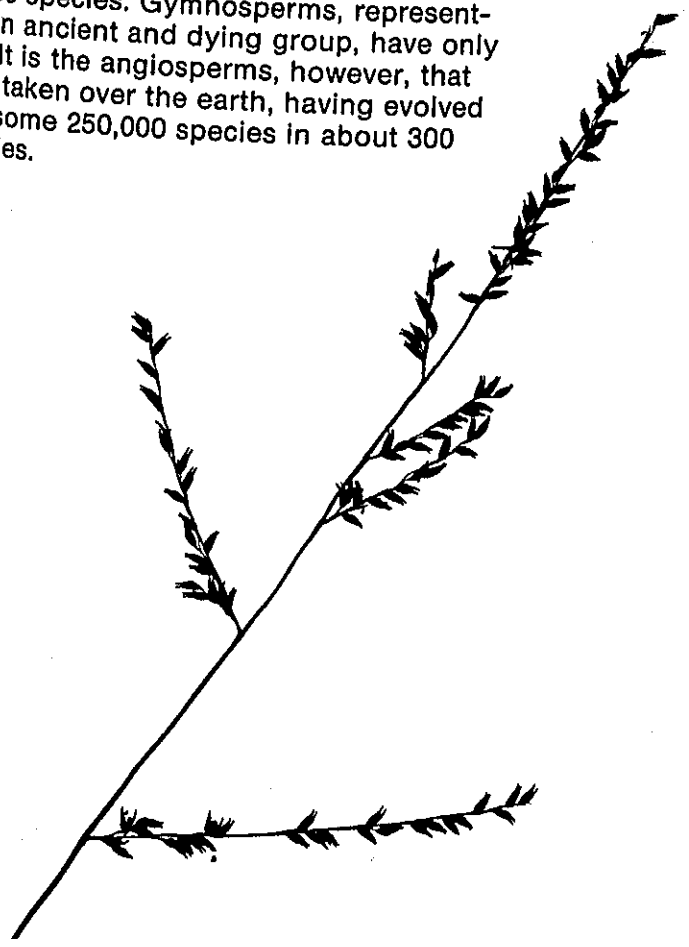
Peoples whom we have chosen to consider members of societies less advanced than ours have consistently looked to the plant kingdom—without which no animal life could have evolved—for food, medicine and other ameliorants of life. With so many varied and sophisticated means at our disposal, should we not take a lesson from them?

No botanist can give a certain estimate of the size of the plant kingdom. Modern guesses vary between 250,000 and 500,000 species. In 1753, Linnaeus, father of systematic botany, named fewer than 10,000 species, stating that the size of the plant kingdom hardly reached this figure. A century later, the English systematist Lindley calculated that there were some 100,000 species in 8,900 genera. Now, only 200 years after Linnaeus' monumen-



tal work, there is a growing belief among botanists that all previous estimates have fallen far short of the true picture.

Contemporary specialists believe there may be between 30,000 and 100,000 fungi, with one expert asserting that the grand total may exceed 200,000 when adequate collections from the tropics are made. Algae are now calculated to comprise from 19,000 to 32,000 species. The poorly known group of lichens numbers between 16,000 and 20,000. Bryophytes—mosses and liverworts—have been neglected but are now estimated at 14,000 to 25,000 species. The pteridophytes—ferns and their allies—can count some 12,000 to 15,000 species. Gymnosperms, representing an ancient and dying group, have only 675. It is the angiosperms, however, that have taken over the earth, having evolved into some 250,000 species in about 300 families.



What have people done with this great assemblage of diverse organisms? Really very little.

People have been around for a million and a half—perhaps two million—years. Their prime necessity during all this time has been food. They instinctively turned to the plant kingdom as the main source of nourishment. Yet they have used as food—even emergency food—only some 3,000 of perhaps half a million species. Of these, only 150 have ever been important enough to enter world trade, and only a dozen or so actually stand between mankind and starvation. How many minor food plants are used in primitive societies in far-off corners of the world unheeded by or unknown to modern civilization?

People have done little better when medicines are considered. The number of plants employed for their biodynamic properties—as medicines, stimulants, narcotics—is legion. Yet sophisticated societies still plod through the mire of apathy in their study of aboriginal knowledge of plant properties. Primitive societies have lived intimately in association with their ambient vegetation, and the experience of millenia has allowed them to amass an astonishing amount of knowledge which, in the hands of modern science, might often provide valuable short cuts in the search for new therapeutic agents. Aboriginal societies everywhere are fast disintegrating or disappearing. We can no longer afford to ignore reports of an aboriginal use of a plant merely because it falls beyond the limit of our credence. To do so would be tantamount to closing a door, forever entombing a peculiar kind of knowledge with the culture that gave it birth.

To substantiate the need to avoid this kind of error, all we must do is review the so-called wonder drugs discovered since the 1930s, several of which have revolutionized many aspects of modern medicine: the muscle relaxants from South American arrow poisons; penicillin and the host of other antibiotics, mainly from fungi; rutin from several species; cortisone precursors from sapogenins of sundry plants; hypertensive agents from our false hellebore; reserpine from the Indian snakeroot; cytotoxic principles from the periwinkle, the May apple and other sources; hesperidin from citrus plants; bishydroxycoumarin from our sweet clover—not to

mention promising compounds from marijuana that are currently attracting attention as potential new medicine agents. This list does not include the curious new psychoactive constituents isolated from some hallucinogenic plants which may prove of value in experimental or therapeutic psychiatry.

Most of these wonder drugs were products of plants that had some biodynamic use in primitive societies. Even the antibiotics—discovered almost by accident in a laboratory during the 1930s—might have been known much earlier if curious reports of the therapeutic use of fungi in ancient Egyptian literature and in medieval herbals had been heeded.

There are many ways to study the plant kingdom and its biodynamic species for new medicinally valuable agents. The most obvious is probably a random or semi-random screening of plants. This method is direct but extraordinarily expensive in time and money. Yet it has been employed in several recent surveys, especially those concentrating on specific constituents such as alkaloids. One American drug firm examined some 40,000 species for alkaloids over a 10-year period. Other surveys are chemically more general but geographically limited. Such surveys have been carried out on the floras of Australia, New Guinea, West Africa, India and other countries. Still other random surveys have concentrated on searching for plant constituents active in certain diseases or for very definite biological properties. Thus there have been surveys for antiviral, antibacterial, and cytotoxic effects, as well as many other properties. About 50 percent of the temperate zone lichens, for example, have been found to possess acids capable of inhibiting gram-positive bacteria, tuberculosis bacilli and some fungi. One of the world's most ambitious random surveys has been the National Institutes of Health's screening of plants for potential anticancer properties. More than 26,000 extracts from 6,500 species have been tested. But in most cases random surveys demand too great an investment in time, money, and skilled personnel to be practical.

Another common approach is to concentrate research on plants that have been or are mentioned in the literature of ancient and contemporary folk medicine. However, this literature is often diffuse, uncritical and of the nature of hearsay, and is scattered throughout many fields. While much of it is highly valuable and holds still untested material, it is unwise to base too ambitious a survey on these often unreliable data. This has been demonstrated time and again. Yet to disregard the literature, both ancient and modern, would be equally irresponsible.

Our herbaria are rich repositories of untapped information on native uses of plants. Data associated with accurately identifiable specimens have usually been gathered in the field by competent naturalists. The wealth of this material is fantastic. Among the larger herbaria, that in Paris has over seven million specimens; Leningrad and Geneva each have five million; Kew in England counts four to five million; Harvard possesses more than four million. There are data on the native uses of many of these specimens. In the past few years several "herbarium searches" have been conducted. A recent one at Harvard yielded 7,500 reports of food or medicinal uses, a large proportion of which bear investigation by modern phytochemical and pharmacological methods.

Undoubtedly the best method of uncovering new biodynamic plant chemicals with medical potential is direct ethnobotanical work among peoples who still preserve all or much of their native lore. Activities of this kind are taking place in various parts of the world, but their progress is hindered by a dearth of properly trained experts capable of searching out such recondite information.

My whole professional life as a botanist has been devoted primarily to a search for potential new drug plants. This activity has been concentrated mainly in the northwestern part of the Amazon valley, a poorly explored region with an incredibly rich flora of over 70,000 species and still unacculturated Indian tribes utilizing plants valued by their forefathers for many centuries.

I lived 14 years in the region—from 1941 through 1954—and have returned at least once a year since then. A total of 2,300 plants were collected. So far, we have identified more than 1,300 species used for medicines, poisons or narcotics. Most of these have never before been reported as biodynamic plants, and very few have been chemically investigated. Here is a wealth of knowledge awaiting the searchlight of modern scientific scrutiny.

While there are undoubtedly many comparable parts of the world, I am constrained to relate some of the striking discoveries from my own sphere of activity. They represent only a small fraction of the many interesting and significant native uses uncovered during my studies.

When delving into the so-called medicinal plants of the northwest Amazon, we must always bear in mind that "medicines" with psychic powers are often more important to the natives than those with purely physical properties. This apparent anomaly is easy to understand. Illness and

death are attributed to the intrusion into the body of malevolent forces from the spirit world. What more logical way, then, to diagnose and even treat illness than to contact these spirit forces? There is in the ethnopharmacopoeias of most American aborigines one or more plants capable, through a variety of hallucinations, of transporting a medicine man or even a patient to the spirit realms, to communicate with the sources of evil. These plants are the hallucinogens—the medicines *par excellence* of the natives.

The Aztecs had perhaps the greatest number of these extraordinary mind-altering plants, and accorded them the highest regard in their magico-religious and medical practices. The peyote cactus, *Lophophora Williamsii,* was the most important. Its use survived intense persecution by the Spaniards and has even spread in a modern religious cult as a sacrament among over a quarter of a million faithful Indians in the United States and Canada. The dried top of this spineless napiform cactus is ingested. It contains more than 30 alkaloids, one of which—mescaline—is responsible for the extraordinary kaleidoscope of brightly colored visual hallucinations induced by this narcotic. Auditory, tactile, olfactory, and gustatory hallucinations are caused by some of the other alkaloids. After four centuries, there is still much to learn about peyote. We are also discovering that the Mexican Indians know and use other cactus species for a variety of intoxications—species only now being subjected to examination by sophisticated chemical techniques.

Another curious hallucinogen of ancient Mexico still in use is ololiuqui, identified only during the past 30 or 40 years as a morning glory. Two species are involved: *Turbina corymbosa* and *Ipomoea violacea.* The seeds of both are employed for sacred intoxicants in southern Mexico. An extraordinary biochemical and chemotaxonomical discovery is that the active principles are ergoline alkaloids, hitherto known only from lowly fungi of the Ascomycetes, especially ergot, *Claviceps purpurea.*

Mexicans also employ a variety of mushrooms as sacred intoxicants. At least 24 species in *Psilocybe, Panaeolus, Stropharia,* and *Conocybe* are known to be used in southern Oaxaca at the present time. The early Spanish chroniclers were greatly disturbed by the religious use of these "diabolic" mushrooms, and persecution drove the cult into hiding. It has emerged only in the past 45 years. The use of divine mushrooms goes far back in history. They are engraved on the Aztec God of Flowers, Xochipili, dating from about 1450 A.D. In Guatemala "mushroom stones" going back to 1,200 B.C. indicate their use as elements of a religious cult at least 3,000 years ago.

One hundred and thirty years ago in Chile a German botanist collected a virulently toxic narcotic called latué, or arbol de los brujos—the solanaceous *Latua pubiflora.* It was used by Mapuche Indian witch doctors. Nothing more was known about this plant, which grows only in one valley of central Chile, until one of my students visited the locality. The plant is no longer used because the Indians have disappeared, but shepherds living there still fear it. It has very high percentages of the powerful alkaloids hyoscyamine and scopolamine.

Another recently discovered South American hallucinogen is the San Pedro cactus, *Trichocereus Pachanoi,* which contains mescaline. It is the basis of a moon-oriented magico-religious cult. The

discovery of ceramic pots in Peruvian graves going back to 1000 B.C. indicates the substance was used in ancient times. These pots depict stems of the cactus with the face of the jaguar, in South America associated with hallucinogens.

Another ancient hallucinogen only very recently discovered is the Amazonian snuff known as yakee, epena, or nakwana. It is prepared from the blood-red resin in the bark of several species of the genus *Virola* of the nutmeg family. Used extensively in the northwest Amazon and upper Orinoco basin, yakee has excessively high concentrations of several tryptamines—up to 11 percent, eight percent consisting of highly psychoactive 5-methoxy-N, N-dimethyltryptamine. The resin is also applied to darts and arrows as a poison, but the chemical constituent responsible for its efficacy in killing animals has not yet been explained.

In the mountains of Chile and Peru grows a beautiful six-foot red lobelia called tupa. Its scientific name is *Lobelia Tupa*. There are indications that this plant, known also as tabaco del diablo (devil's tobacco) may be hallucinogenic, but much more field research is needed before it is fully understood.

Before discussing the physically active medicinal plants, it is important to mention the medicinal potential of one of the oldest and most widely employed hallucinogens: *Cannabis sativa* or marijuana. This ancient cultigen, a five-purpose species, has been assiduously studied by chemists and pharmacologists in recent years because of the great increase in its use as a narcotic in Western society. We now know there are at least 50 distinct cannabinolic compounds in this plant, which is a veritable chemical factory. Many of these may have medicinally valuable properties. In the hands of synthetic chemists, they can yield a myriad of semi-synthetic compounds never before known. It is highly likely that modern medicine will find these new substances of interest, since recent research has already indicated the value of some *Cannabis* compounds in treating glaucoma and alleviating suffering in cases of terminal cancer. One of the five uses of *Cannabis* throughout human history has been as a medicine. Until 1937 it was listed in the *U.S. Pharmacopoeia* as a sort of tranquilizer, and may soon be included again.

For centuries South American aborigines have hunted and warred with curare—arrow poisons made primarily from species of *Strychnos* or from several genera of *Menispermaceae,* the moonseed family.

Of special interest to modern medicine are those arrow poisons prepared from menispermaceous plants, which act on the muscles. The genera involved are *Abuta, Chondrodendron,* and *Curarea.* The active principle—tubocurarine—is now a major medicinal compound in thousands of hospitals. The source of these plants is still the natives of the western Amazon who gather the material from the jungle lianas and elaborate it in their rustic homes for sale to representatives of pharmaceutical establishments.

The study of arrow poisons, many of which may have significance for modern medicine, is just beginning. Research has uncovered plants basic to arrow poison recipes in diverse families. Most of these are chemically unknown and of potential medicinal interest.

Arrow poisons made from menispermaceous species as well as those prepared from *Strychnos* are well investigated. There is, however, a wealth of new chemical discoveries to be made when the minor curare plants are fully researched.

One hundred and fifty years ago, von Martius, the German plant explorer, reported that Amazonian Indians of Brazil and Colombia prepared a curare from the annonaceous tree *Unonopsis veneficiorum.* We have rediscovered this rare tree as the source of the basic ingredient in an arrow poison used by the Kofán Indians of Ecuador. Another new type of arrow poison is elaborated by these same Indians from the lauraceous *Ocotea venenosa,* a plant containing bisbenzylquinolinic alkaloids. The flacourtiaceous *Mayna amazonica* is likewise an ingredient of the arrow poison of the isolated and primitive Kofán Indians. The bark of *Connarus opacus* and *C. Sprucei* have recently been reported as ingredients of the arrow poison preparations of the Witotos of Colombia. Another newly reported and pharmacologically uninvestigated arrow poison plant used by the Taiwano Indians of the Colombian Amazon is made from the bark of *Ormosia macrophylla* together with the bark of *Vochysia ferruginea* and the crushed stems of an aroid (possibly a species of *Philodendron*).

Interesting new types of fish poisons have recently come to light in South America. The fruit of a species of the rare genus *Caryocar,* crushed and mixed with mud, represents a principal piscicidal preparation of the Indians in the Colombian Vaupés. Two species of *Philodendron* are used for the same purpose in this area. The Desano Indians cut and bundle leaves of *P. crasspedodromum* and allow them to ferment and rot for several days, whereupon they are macerated and cast into still water. Another species of *Philodendron,* still not described, is similarly utilized in a different area of the northwest

Amazon. Nothing is known of the chemistry of these aroids.

A fascinating new species of the bombaceous genus *Patinoa (P. ichthyotoxica)* represents a rare minor fish poison of the Tikuna Indians. The pulp of the large fruit is dried and kept for use throughout the year—cast upon still water to stupefy the fish. The Kofáns employ the very rare *Schoenobiblus peruvianus,* one of their arrow poison plants, as a fish poison. Many other plants have recently been discovered as fish poisons, but their chemistry is unknown: *Conomorpha lithophyta, Mendoncia aspera,* etc.

The Indians of the northwest Amazon avoid a great many plants because of their toxic properties. Yet we knew nothing of their chemical constitution. That they are poisonous indicates they possess active constituents, some of which may be of value to us in medicine or industry.

I also want to mention a few of the many plants with presumed medicinal value to indicate the wealth of knowledge these natives have regarding the flora of their environment.

The lowly *Schiekia orinocensis,* relative of our own bloodroot, is prepared in a potion thought to restore youth to the aged. Several species of the beautiful solanaceous genus *Brunfelsia* have curious chemical constituents, not yet elucidated, which cause chills when drunk in the form of tea. For this reason, the plants are highly valued as febrifuges and, in the Kichwa language of the western Amazon, are called chiric-caspi or "chill tree." These species are also employed by the natives as hallucinogens.

The Kubeos of the Vaupes use an astringent tea of *Aristolochia medicinalis* to treat individuals who suffer from frequent attacks which may be epileptic.

One of the most prevalent problems in the Amazon regions is conjunctivitis. Two plants are widely used to treat this condition. The yellowish leaves of the bignoniaceous vine *Arrabidea xanthophylla* are prepared in an infusion. The Indians of the Apaporis basin cultivate a special plant of the squash family for this purpose *(Cayaponia ophthalmica).*

An interesting plant, the red saprophyte *Helosis guyannensis* of the *Balanophoraceae,* provides the Tikuna Indians with a hemostatic powder said to help congeal blood flowing from deep wounds. Whether or not its apparent effects are due to the fine powder made from the dried plant in increasing surface or to some active ingredient is not yet known.

A very common complaint in the wet, hot tropical Amazon is fungal infection of the skin. I have discovered that a number of species are used in the form of a wash, or the red resinous liquid of the bark is applied directly, to cure fungal and other skin infections or to cleanse infected wounds. These plants belong mainly to the myristicaceous genus *Virola.* Recently a Brazilian chemist, who studied several species of *Virola,* reported that they do indeed contain chemical compounds capable of fungicidal activity.

During my years of botanical exploration in the northwestern Amazon, I encountered three plants used in the belief that they have properties making them valuable as oral contraceptives: *Philodendron dyscarpium, Urospatha antisyleptica,* and *Anthurium Tessmannii,* all members of the *Araceae.* The first two are used by a number of tribes in the Vaupés, the third by the Tikunas in the Colombian Amazonas.

We should not forego mentioning the very great value in the Amazonian economy of the coca plant, source of cocaine. It is used daily as a drug. The powdered leaves are mixed with an alkaline ash admixture of leaves of a species of *Cecropia.* The drug is chewed for its stimulant effect. The plant is a semisacred element of all Indian cultures—*Erythroxylon oca* var. *Ipadu.* It is also used in the Andes, but does not have the sacred character accorded it in the Amazon. Although known for many years as the source of cocaine, the plant needs further study in view of recent research, using modern sophisticated chemical techniques.

Many years ago I identified a gigantic jungle liana from whose bark the Indians of the westernmost Amazon of Colombia and Ecuador prepare a cold-water drink with highly stimulating qualities. It is called *Paullinia Yoco,* after the aboriginal name of the plant, yoco. The bark contains three percent caffeine. It is the only caffeine product known which is prepared from bark. These Indians, especially the Kofáns, are so dependent on yoko that, when the wild source is depleted near their villages, they simply pick up and move to a more propitious location.

Several curious species of *Souroubea* of the rare family *Marcgraviaceae* are used over a wide area as the source of teas taken as tranquilizers, to cause drowsiness and even to induce sleep. We know nothing yet about the chemistry of these interesting plants.

Along the flooded banks of the Amazon River, one of the most conspicuous plants is an aroid that may reach a height of 30 or 35 feet: *Montrichardia arborescens.* The root is boiled to make a strongly diuretic tea.

I'll conclude by mentioning only two of the many plants of the high Andean moors or *paramos* of Colombia that merit

more phytochemical examination. There are many species of *Espeletia,* a giant composite sometimes attaining a height of 25 or 30 feet. The resinous leaves of these odd plants, which occur in dense stands above 10,000 feet, apparently have beneficial properties for patients with flu or bronchial congestion. They are burned, and the heavy resin-laden smoke is inhaled, seemingly with excellent results.

Another unusual plant of the high moors is *Puya,* a genus of the pineapple family. Some species attain a height of 30 feet. From the flowering stalk of this plant, a tea is made which is said to help aged people who are losing the ability to walk at high altitudes between 12,000 and 13,000 feet. Surprisingly, there are indications that the flowers of *Puya* contain an alkaloid.

Let us all remember that the botanist does not have to go to far-off exotic places to find new medicines from the plant kingdom. Two valuable drugs only recently discovered come from plants of our own limited flora of northeastern North America. The May Apple, *Podophyllum peltatum,* has given us podophyllotoxin, found to be valuable in treating uterine warts, and is currently under study as a possible antineoplastic compound with potential anticancer properties. The second is False Hellebore, *Veratrum viride,* source of valuable hypotensive agents.

It would be futile to continue a recitation of the many species reported to be medicinally used by the Indians but which have not yet been investigated. The only sure thing is this: the plant kingdom is an untapped emporium of new and potentially significant medicinal compounds.

What of the future? How much longer will this fund of ethnopharmacological lore be available for us to tap in our search for medicinal plants?

The future looks dim. What we euphemistically call civilization is on the march everywhere, and its pace is now accelerated. Wars, tourism, the construction willy-nilly of roads, increased commercial and missionary activities are penetrating vast areas, especially in tropical America—areas hitherto more or less virgin and left to primitive societies, if indeed they were inhabited at all. Our political leaders equate "progress" with destruction of natural resources. To many of them, the forest is an obstacle to be removed.

What primarily concerns ethnobotanists is the progressive divorcement of primitive peoples from dependence on their immediate ambient vegetation. Even if they are not exterminated or eliminated by racial and cultural absorption, the arrival and cheap availability of aspirin and quinine tablets, for example, seem often to start an astonishing disintegration of native medicinal lore. The rapidity of this disintegration is frightening. Whether aspirin may be more efficient than native herbal remedies and magic is not ours to consider here. What does interest and worry us is the almost certain loss of the greater part of America's nature herbal lore in the next half century. Our search among the plant kingdom's half million species for new medicines will then have lost a most valuable and promising field of exploration.

I cannot refrain from ending with a delightful and greatly foresighted quotation from Carl Linnaeus who, in the late 1700s, said the following which we must heed today:

> Man, ever desirous of Knowledge, has already explored many things: but more and greater still remain concealed; perhaps reserved for far distant generations, who shall prosecute the examination of their Creator's work in remote countries, and make many discoveries for the pleasure and convenience of life. Prosperity shall see its increasing Museums, and the knowledge of the Divine Wisdom, flourish together; and at the same time all the practical sciences ... shall be enriched; for we cannot avoid thinking, that what we know of the Divine works are much fewer than those of which we are ignorant.

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