The Geography of Drugs

By RALPH W. CLARK

White and Foscue have defined geography as that subject which is "concerned with nature (physical and biological) as it provides an environment only for man." Drugs have been defined by the Federal Food, Drug and Cosmetic Act of 1938 as "articles intended for use in the diagnosis, cure, mitigation, treatment or prevention of disease in man or other animals." Drugs are derived from the mineral, vegetable, and animal kingdoms, or they are prepared synthetically. Space requirements will limit this paper to a discussion of only a few of the many crude vegetable drugs. These vegetable drugs may be used in their raw form, as ground or unground plant parts, or as sources of derived substances.

Conditions of climate and soil are of primary importance in the distribution of both indigenous plants and the successful cultivation of introduced foreign species. Frequently, the chief geographical source shifts, because of various influences, such as a change in climate, the success of introduced species elsewhere, derangements caused by war, or through neglect by the inhabitants of a region.

The synthetic production of the active principle of a drug usually reduces the industry's demand for the crude drug, although at the same time there are those who will still prefer the natural product. The synthetic production of ephedrine is so successful that the extraction of ephedrine from ephedra, better known as Ma-Huang, has been greatly reduced. However, 46,095 pounds of ephedra still were imported from Yugoslavia and Pakistan in 1952. Ephedrine from MaHuang was introduced to the medical profession only slightly more than twenty-five years ago by Dr. K. K. Chen, then of the Peking Union Medical College. The crude drug had been known to the Chinese for many centuries. In 1938 ephedrine was synthesized by Merck & Co., Inc., at a price which made further extraction of the drug impractical.

Ephedra of various varieties was known to exist at many points throughout the world, including China, India, Spain, Poland, and certain sections of southwestern Oklahoma and our Far West. It was necessary for Eli Lilly & Co., a very large early producer of ephedrine products, to determine at that time which drug source produced the greatest yield of alkaloids. Arrangements were made to gather substantial amounts from the various localities of India and the other countries mentioned. The results of this work definitely determined that the Chinese drug was higher in alkaloid content than that derived from other localities. It was also discovered by monthly gatherings in the same area near Tientsin that the drug at maturity during July and August yielded an alkaloid content approximately three times higher than during other parts of the growing season. Only one-third of the tonnage of the drug was imported after this investigation than before.

The use of synthetic methyl salicylate has replaced the more expensive similar natural product obtained by maceration and subsequent distillation with steam of the leaves from *Gaultheria procumbens* or the bark from *Betula lenta.* These grow in eastern North America from Ontario, Canada, to New England and North Carolina. Methyl salicylate must be labeled to indicate the source, since some variation occurs in the liquid product, caused by a content of 2% "impurities" which, dependent on the source, are not methyl salicylate. These so-called impurities impart a taste valued highly by the connoisseur of fine wintergreen flavor. They do not affect the medicinal value of methyl salicylate. That is not true of ephedrine, as this chemical does not vary with the source. Camphor may be obtained from *Cinnamomum camphora,* which grows in Formosa and Japan, or can be produced synthetically. The producer is not required to declare the source on the label, indicating that, like ephedrine, there is no easily distinguishable nor important difference between the synthetic and the "natural" product.

The commercial source of a drug may be the country or region to which the drug is indigenous and may even make up part of the scientific name, as in the ripe fruit of *Olea europaea* from which olive oil is obtained. Sometimes the common name reflects the range of a drug, as *English valerian,* which is grown in England. In a number of cases the port from which the drug is shipped, rather than where it grows, enters the name, as *Peruvian balsam* shipped from Lima, Peru, but grown in San Salvador. Sometimes the scientific name is misleading, as showing the principal habitat of a drug; for example, supplies of *Hydrastis canadensis* are obtained almost entirely from plants cultivated in the states of Washington and North Carolina, not Canada, and *Prunus virginiana* which may be found throughout eastern and central North America instead of being limited to Virginia.

In the United States the three regions of crude drug production are roughly the Pacific Northwest, the Midwestern Farm Belt, and the Southeast. Crude drugs are obtained in the Pacific Northwest by collection from indigenous wild plants (cascara —3 to 8 million pounds), or cultivated, introduced plants, (digitalis, peppermint, hydrastis, etc.) The products of the Midwestern Farm Belt, principally Ohio, Indiana, Illinois, Michigan, and Wisconsin, are largely volatile oil-bearing plants produced from large acreages. The production of peppermint and spearmint oils averages 1,410,000 pounds per year. Approximately two-thirds of this quantity is grown in Michigan and Indiana, with one-third in Oregon and Washington. The numerous items from the Southeast are from wild plants collected, more or less sporadically, by men, women and children chiefly in the Blue Ridge and the Great Smoky Mountain regions of Virginia, West Virginia, North Carolina, Tennessee, and Kentucky. A very interesting article entitled "Carolina Herb Woman" appeared in the December 6, 1952, issue of *Colliers.* Mrs. Lula Miller, the herb woman, and her children collect drugs to sell to the Greer Drug Company, which has a warehouse in Lenoir, North Carolina. The firm buys 150 different herbs and barks. It sells tons of crude drugs to American pharmaceutical houses and exports some, too. However, the total export of this and other suppliers of crude drugs from the United States is small. On the other hand, botanical products (crude drugs and products from them), have ac-

counted for approximately $100,000,000 as compared to $243,968,997 of chemical, medicinal, and allied products imported in 1952. Drugs with alkaloidal content have increased in use, but they are few in number, while many drugs formerly known as old standbys have fallen by the wayside. A long-line pharmaceutical manufacturer used several hundred different crude drugs at the turn of the century, as compared to only two or three dozen now.

One of the vegetable drugs about which some of us may have unpleasant memories is ipecac. It is still imported in considerable quantities—54,559 pounds in 1952 from Nicaragua, Costa Rica, Panama, Canal Zone, Colombia, and Brazil.

Ginseng is another interesting drug. We imported 222 pounds from Canada in 1952, at a value of $3,043. It is used by the Chinese as a panacea for a great variety of diseases.

THE IMPACT of war on the importation of crude drugs, and its stimulating effect on the search for new sources of supply, is well illustrated in a portion of a letter to the author from Mr. A. H. Brown of Eli Lilly & Company, dated December 30, 1952:

"During World War I, the manufacture of atropine sulfate was dependent entirely upon supplies of belladonna leaves originating in central Europe. Being deprived of this source and due to the fact that atropine was urgently needed for ophthalmic examination, we attempted to produce substantial quantities of atropine for the Allied Armed Forces from stramonium leaves or jimpson weed which grows in profusion throughout the entire Middle West. The percentage of alkaloids contained in these leaves is extremely small, but due to the quantities of this material which are available and utilizing the adsorption process of the late Dr. John Uri Lloyd, we were able to produce a sufficient amount of atropine to take care of the world supply. The price was necessarily much higher than if belladonna had been utilized but, even so, adequate supplies were maintained. There was, of course, a pharmaceutical need for belladonna leaves which could not be satisfied by stramonium, and this we undertook by cultivation at our farm at Greenfield, Indiana, with some success. It was necessary to grow the plants with seeds under glass and transplant the seedlings into fields until proper growth was obtained. This was necessarily costly and at the close of the war, our efforts were discontinued due to the return of the foreign drug of wild growth, and in addition, we furnished seed at no cost to the government and to numerous private individuals who raised a sufficient amount during the period of the war to take care of our entire needs and largely the entire needs of the country.

"Henbane, another essential drug, was practically unobtainable during World War I as a source of scopolamine. Apparently, it was unknown at that time that there are abundant quantities of this drug in western Montana where it can be harvested mechanically and in sufficient quantity to satisfy world needs. This was practiced during World War II, so that no shortage existed during the period of the emergency and also during that period, from sources unknown to the writer, scopolamine became available from Australia at very low prices and in sufficient quantities to take care of the needs of the Armed Forces. This is particularly mentioned inasmuch as scopolamine was the basic ingredient of the motion-sickness tablets that were used by all Allied personnel participating in the Normandy invasion. [Incidentally, the U. S. imported 117,014 pounds of henbane in 1952 from Belgium, West Germany, Hungary, and Egypt.]

"As we are one of the largest extractors of ergot alkaloids, we have for many years had a substantial interest in this drug, originating with the introduction of ergovine maleate to the medical profession about 25 years ago. At that time ergot was largely derived from the rye harvest of Russia and Poland with some supplies reaching this market from Spain and Portugal, but with the coming of the Russian Revolution, supplies from eastern Europe were entirely cut off, which placed total dependence upon Spain and Portugal for world supplies. The supplies from those two countries were totally inadequate for world needs and, as a result, intensive speculation dominated the market for many years. In fact, prices ranged from a low of 18 cents per pound to a high of $10.00, which prevailed during 1952. In order to free ourselves of foreign domination in this market, we began an intensive educational and promotional effort to have the ergot saved from the American and Canadian harvests, where it had heretofore been sifted out of the rye grain and destroyed as a harmful parasite.

"Through the medium of druggists, doctors, grain elevator men, farmers, county agricultural agents and agricultural teachers in the county schools, we were able after a year or so to create an interest in the saving of ergot to a point where the amount of ergot obtained was equal to the entire United States imports in many previous years. Today, the saving of ergot is regular procedure in grain and terminal warehouses, as well as at the elevators and farms, with the result that Portuguese speculation has been broken and prices have been substantially reduced over those which had prevailed a year or so ago. We feel that in this particular work our efforts have been very effective and have freed this country from any ergot shortage in times of war or crop failures abroad."

Nevertheless, the imports of stramonium and ergot remain quite large. The importation of stramonium from Argentina, Hungary, Yugoslavia, and India was 225,420 pounds in 1952. We imported 238,871 pounds of ergot in 1952, mostly from Portugal and Canada, at a value of $756,976. The 122,371 pounds which came from Portugal had a value of $603,193 as compared to a value of $146,380 for the 114,373 pounds from Canada. Ergot is also cultivated in Germany and Rumania.

AT THE PRESENT time special interest is being shown in the antibiotics. They, too, offer an interesting chapter in the geography of drugs. Dr. Rene J. Dubos extracted tyrocidin and gramicidin. Later, however, pure gramicidin-S was discovered and secured from Russian soil; streptomycin was first isolated from New Jersey soil; terramycin came from one of several thousand soil samples—this one from Aus-

About the Author

Dr. Ralph W. Clark became Dean of the College of Pharmacy in 1949. His training and experience for the position had been extensive and diversified. Educated at the University of Wisconsin, he had worked in both retail and hospital pharmacies. For several years he had been director of the pharmacy service department of Merck & Co., Inc. He had served ten years on the staff at Wisconsin, and later had been Professor of Dispensing Pharmacy at the University of Kansas. He is a member of many pharmaceutical organizations, and has published articles in American and Canadian professional journals. He was the first editor of the Wisconsin Druggist. *Many changes have been made in the College of Pharmacy in the last six years, but the emphasis continues to be placed on preparing graduates for employment in Oklahoma retail drug stores.*

tralia. Polymyxin was found in an English garden; penicillin was also discovered in England, but one of its better strains came from a rotten cantaloupe in Peoria, Illinois. One of the newest antibiotics, ilotycin or erythrocin, brands of erythromycin, was isolated from soil taken from the Philippine Islands. The report is that chloromycetin was elaborated from two isolates: one from near Caracas, Venezuela, and the other from the vicinity of Urbana, Illinois.

J. B. Routien and A. C. Finlay, of the Biochemical Research Laboratories of Charles Pfizer, point out that antibiotics have been isolated from compost, decaying vegetable matter, lake mud, and other miscellaneous materials. The most common source, however, has been soil. The choice of soils appears to have been at random, some investigators using local soils and others preferring world-wide collections.

The magnitude of the task of adequately examining soils for desirable micro-organisms, becomes apparent when we consider an area such as the continental United States. Any one of its 1,903,000,000 acres might, theoretically, contain a desirable culture which has arisen by mutation. In addition to this, one can point out irradiation of spores of actinomycetes. As a matter of fact, the present strain of penicillin is a mutation of the penicillin grown on the rotten cantaloupe in Peoria, Illinois.

In spite of the supremacy of the antibiotics in medicine, the cost estimated at over $500,000,000 per year, including about 10 per cent of exports, morphine is considered by many to be the most important drug as a pain reliever. The estimated world production of opium, from which the chief product is morphine, is 1,900,000 pounds. Of this quantity, over 897,779 pounds, representing 100,851 pounds of morphine, were imported into the United States in 1952, with a dollar value of $6,889,300. Several attempts have been made to cultivate the opium poppy in the United States, but so far the resultant crude opium has had a very low morphine content.

The opium production of the world centers chiefly in Asia, especially in China, India, Iran (Persia), Asia Minor, and Afghanistan. It is also found in French Indo-China, Semiretchie (in Asiatic Russia), Korea, Japan, Turkey, Yugoslavia, and Bulgaria. Greece at one time was a major producer, but the culture of the opium poppy has been discontinued. China today is by far the largest opium grower and consumer, but the product is not of medicinal quality. The principal countries supplying opium for medicinal and scientific needs are Turkey, Iran, and India. Opium from all other countries is low in the percentage of the desired active ingredient—morphine.

Demerol and methadone are synthetic drugs with morphine-like action. They are extremely important as factors in stabilizing the supply of analgesic drugs, the most important of which is morphine. The importance of the synthesis of these drugs cannot be over-estimated because, for the first time, man has achieved his independence from opium in the relief of severe pain. New drugs with morphine-like action but which will not cause addiction are the subject of extensive research by the pharmaceutical industry, and we may hope for success in the not too distant future.

It is probable that Hippocrates (460-359 B.C.) relied on two drugs which since the dawn of history have been used to produce sleep. They are opium, discussed above, and mandrake (*Atropa mandragora*) a perennial European plant which is often compared to the human form because its twin roots suggested human legs. In former times the root of this plant was supposed to possess magical values. It was administered as a wine to produce sleep. Now the pharmaceutical chemist gives nature a hand.

The chief constituent of belladonna is atropine. The plant *Atropa belladonna* is native to Southern and Central Europe. Although it has been cultivated in the United States (Michigan, New York, Washington, and California), England and France, the main supply from both cultivated and wild growth comes from Yugoslavia, Italy, and Russia. The United States imports were 357,000 pounds in 1950, 38,186 pounds in 1951, 12,387 pounds in 1952. Approximately 200,000 pounds were imported annually from 1931 to 1940. Several plants of the genus *Datura,* especially *Datura stramonium,* also are the source of atropine. *Datura stramonium* is probably indigenous to the region of the Caspian Sea. It has been naturalized in Europe and the Americas. It grows throughout the temperate world. A considerable quantity of the drug is produced in the southeastern part of the United States. We imported 225,420 pounds in 1952 from Argentina, Hungary, Yugoslavia, and India.

Atropine has been prepared synthetically but up to the present time, commercial synthetic production has not been feasible. Homatropine is a product of somewhat different chemical formula which modifies the atropine-like action. It is made from tropine and mandelic acid. Another synthetic product, syntropan, has been developed for more specific (in some respects, atropine-like) action. Trasentine and pavatrine act similarly to syntropan, although they differ considerably chemically from syntropan. Other synthetic drugs have also reduced the use of atropine. They represent improvements over the natural products, both from the point of view of a dependable source of supply and of modified action, which emphasizes the desirable medicinal properties and diminishes the "side effects."

Most of the very important drug, digitalis (foxglove), used in the United States is now produced domestically. This drug plant is indigenous to England. Plants also grow wild and are cultivated in New England, New York, Minnesota, and the Pacific Northwest. The European source is chiefly the Balkans, Ceneral Europe (Germany), and England. Digitalis was used in domestic medicines in England as far back as the tenth century, but it was not introduced into regular medical practice until 1775 by Dr. Withering. Little was known concerning its active principles until Nativelle discovered the potent glycoside digitoxin in 1871. In current medical usage, this and other digitalis glycosides are usually preferred to the drug or the tincture of digitalis.

Nux vomica is a button-form seed from *Strychnos Nux-vomica.* This strychnine-yielding drug is native to coastal forest areas of India. Imports from India were 1,159,956 pounds in 1952, most of which were used for purposes other than medicinal.

South American (from Brazil and Peru) species of *Strychnos* are the source of curare, an important drug in causing muscular relaxation for abdominal surgery. It has been used extensively only during the last ten years. At a very early date South American Indians used it as an arrow poison.

The U. S. imports of gentian were 246,658 pounds in 1952 from France, Spain, and Yugoslavia. Imports of licorice were 39,718,304 pounds in 1952, from West Germany, Russia, Italy, Turkey, Syria, Iraq, and British East Africa. This $1,669,880 import has many uses, only a small part of it in pharmaceutical products.

Only three vegetable drugs, in addition to cascara, previously mentioned, remain relatively important as laxatives. They are senna, rhubarb, and aloes. Senna imports from Egypt and India amounted to 1,798,662 pounds in 1952. Rhubarb is imported from China and India. The quantities imported were 407,011 pounds in 1950; 93,790 pounds in 1951; 3,608 pounds in 1952 (from India). Aloes imports were 413,847 pounds in 1952 from Dominican Republic, North Antilles, Venezuela, and Union of South Africa.

THIS ENTIRE paper could have consisted of a review of *Jungle Memories,* a book by Henry H. Rusby, and the discussion of two very interesting and very important South American drugs: coca (source of cocaine) and cinchona (source of quinine). Dr. Rusby planned his expedition over the Andes and down the Amazon River many years ago while he was employed by Parke, Davis & Co. His assignment in this botanist's paradise was to secure supplies of known drugs and to search for new drugs. Dr. Harry E. Hoy, Chairman of the Department of Geography of the University of Oklahoma, has taken nearly the same route—but as a geographer. I wish I had been privileged to sit in on a conversation between these two men, had it occurred, since they had covered somewhat the same region but with two different purposes in mind.

The dried leaves of *Erythoxylon coca* and related species are extracted for cocaine, a local anesthetic. Coca plants have been cultivated by the Indians of the Upper Andes of Bolivia, Peru, and Colombia for several centuries. Coca, "the divine plant of the Incas," was honored in sacred ceremonies of the natives everywhere. These people derived increased physical stamina by chewing the dried coca leaves. Dr. Rusby expresses the opinion that the drug acts to stimulate the respiration in the rarefied atmosphere, and to blunt the sense of physical and mental discomfort resulting from exhaustion. The desire for sleep is also reduced. Although there are accounts of coca chewers who have become addicts, Dr. Rusby found no such case. On the other hand, cocaine does cause addiction. It produces a feeling of elation and euphoria, which is followed by a period of depression and tremors. Cocaine hydrochloride or "snow" is injected or snuffed by addicts. Commonly used synthetic local anesthetics with some of the properties of cocaine are: procaine, butacaine, benzocaine, metycaine, nupercaine, diothane, and holocaine. There are many others.

Coca is also grown in Indonesia. For many years the cultivated leaf from Indonesia was the most desirable one for the production of cocaine because of the higher cocaine content (approximately 2%); but the ravages of World War II caused the plantations to be overrun with wild growth almost of jungle proportions. As a result, the leaf is no better than the South American leaf. The Bolivian and Colombian production, as well as a good deal of the Peruvian, was for home consumption where, as previously mentioned, it is used for chewing purposes.

Production figures of coca leaves are not available, but it is safe to say that it is more than 2,000,000 pounds, and could very easily be 3,000,000 pounds.

The exportation of viable seeds from Bolivia is illegal, owing to the desire to prevent foreign competition in the production of coca leaves. South American countries resent intensely the loss of monopolies in various natural products, resulting from the introduction of their cultivation into other countries, cinchona and rubber being notable instances of this fact. Formerly, all cocaine was made in Europe or North America, from imported leaves, but factories have now been established in the region of production for the manufacture of crude or impure alkaloid, which is then shipped to Europe or North America for refining.

To make a creditable summary of the drug cinchona is a very difficult task. The mystery shrouding the discovery of the drug has never been authoritatively cleared. One tradition ascribes the use of the bark to a Jesuit priest. The first authentic record of its use was in 1630 when the wife of the Count of Cinchon was treated for malarial fever by her physician, Dr. Vega. The best source of the drug is the Andean tropics from altitudes of 3,000 to 9,000 feet, or even higher, in Bolivia north to Venezuela. The best natural stands were originally in Bolivia and Peru. From the earliest time, bark collecting of species of cinchona was marked with glaring wastefulness and wanton destruction. The trees were introduced by cultivation into India and the Dutch East Indies, from which source a large portion of this quinine-yielding drug is supplied. The importance of quinine for the treatment of malaria may be understood by the statement that 800,000,000 people annually suffer from the disease and that there are at least 4,000,000 deaths from malaria each year. The urgent need for the anti-malarial, quinine, the first *specific* drug, during World War II, was brought about by the early capture of Java by the Japanese. Java in the last half century supplied 95% of the world's quinine. As a matter of interest, Merck & Co., Inc., largest United States processors of cinchona bark, initiated experimental work on cinchona in Guatemala a decade before the war. The outbreak of the war gave a terrific impetus to plantation activity. Cinchona research has taken a new path in this hemisphere. Successful cultivation and hybridization of cinchonas will depend somewhat on the synthetic anti-malarials, such as atabrine, chloroquine, plasmoquine, pentaquine, and others now available or to come in the future.

The peace-time importation of cinchona is but a small item compared to wartime needs. The importation in 1950 was 441,157 pounds; in 1951, 695,940 pounds, from Central America, the Philippine Islands, and Indonesia. Only 11,200 pounds were imported from Ecuador. In 1943 more than 7,750,000 pounds of cinchona bark were imported into the United States from Bolivia, Peru, Ecuador, and Colombia; and in the three years of 1943-45, the wartime production of Peru alone amounted to over 4,000,000 pounds.

GEOGRAPHICALLY speaking, the world is our garden. Old-world sources of drugs are still foremost, despite attempts to develop American sources of a number of important drugs. Plants, giants in the earth, were not forgotten by Shakespeare. This is what he said about them:

> "O! mickle is the powerful grace that lies
> In herbs, plants, stones, and their true qualities:
> For nought so vile that on the earth doth live
> But to the earth some special good doth give . . ."

In addition to the primary factors of climate and soil and the impact of synthetics, three other factors must be met to a reasonable degree in replacing long-established sources of drugs. They are (1) low wage scale; (2) geo-political stability; (3) accessible transportation. And, finally, every day new leads are obtained which point to the medicinal value of new drug plants, besides bringing some old drugs off the dusty shelves to which they had been relegated. Examples of new drug plants are *Sophora japonica* (200,000 pounds a year), as a source for rutin, and Cabeza de Negra root (Mexican yam), which recently has become an important source of an intermediate in the production of cortisone.

Rauwolfia serpentina (*Ophixylon serpentinum*) has been used in India for many years to treat a variety of diseases relieved symptomatically by a sedative or relaxing drug, such as rauwolfia. This drug, new to us, adds another to the rapidly increasing number of hypotensive drugs which are being used to treat hypertension. The drug and its active principles are used very extensively at the present time. It may be tolerated better than veriloid, the hypotensive extract from another vegetable drug, *Veratrum viride* (American, or green hellebore; habitat, North America). The alkaloids from the root of *Veratrum album* (European or white hellebore; habitat Yugoslavia, Italy, Switzerland, on the Alpine slopes) also are used as hypotensive drugs under the trade names, Protoveratrine A and B. It is reported that 3,000 plants have been imported into Holland in an effort to cultivate the plant there.

The extract of podophyllum (May apple) is an example of an old drug formerly used

as a drastic laxative brought back into use—a different use. During World War II, it was utilized externally for the treatment of certain types of soft warts.

The fragrance of new mown hay curing in the field is well known to everyone. A product called dicumarol, a derivative of the pleasant smelling couramin, is now an important intervenous anti-coagulant, available because Dr. Karl Paul Link of the University of Wisconsin not only observed the odor of coumarin but also studied the bad effect of ingestion of large quantities of curing hay by cattle in the dairy state of Wisconsin. It is a good drug when used in proper quantities, but excessive amounts cause bleeding. It is the active ingredient of warfarin, a rat poison!

Recently, a very active drug has been obtained from rhododendrons: These plants grow extensively in the United States. They are very common in North Carolina. For the present, the drug is being used only on an experimental basis.

In a recent article entitled "Black Magic for Men in White," the author, Don Romero, points out that scientists have discovered active principles in many plants because laymen may have used these plants to treat certain types of illness, wounds, or burns for centuries. As an example, Dr. Boris Sokoloff, in his book, *The Story of Penicillin,* tells of seeing a Serbian peasant who had been gored in the shoulder by a bull. As he stared with horror, the peasant's wife promptly packed her husband's wound with pieces of mouldy bread. "But he will get blood poisoning," protested Sokoloff. "No!" replied the other peasants, "He will get well—we have been using this treatment for generations." Now doctors agree that the substances which were causing these cures might contain antibiotics similar to penicillin and streptomycin. Dr. Thomas Lewis of the revision committee of the U. S. Pharmacopoeia is a strong advocate of research into all kinds of primitive cures. He believes that "Even in this age of synthesized drugs, valuable theories may be lost to medicine if we don't make an exhaustive exploration into those cures which primitives apparently have been able to find in plants." Dr. Waksman, winner of the 1952 Nobel Prize for his discovery of streptomycin, has stated: "Letters are constantly coming to us from all parts of the world telling of strange primitive drugs. Even when these cures sound utterly fantastic, we make every effort to investigate them thoroughly—for we never know when one of them may be the clue to an important discovery." In conclusion, Mr. Romero quotes one pharmaceutical manufacturer as having said, "It sounds incredible that scientists should be 'witch hunting' in the twentieth century, but we never know when we will find a plant which later becomes a household remedy."

Crude drugs, either as such or more often as sources of active principles, will long occupy an important place in medicine, and they will, of course, continue to be important in economic botany and be increasingly seriously considered in discussions of plant geography.

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