Narcotic Plants as Sources of Medicinals, Nutraceuticals, and Functional Foods

Ernest Small

National Environmental Program, Biodiversity Section, Agriculture and Agri-Food Canada, Saunders Bldg., Central Experimental Farm, Ottawa ON K1A 0C6

Abstract

This review examines eight of the world's principal narcotic plants in order to assess their prospects as sources of pharmaceuticals, nutraceuticals, and functional food components. The marijuana plant (*Cannabis sativa*) has already proven to be promising in these respects, particularly with regard to seed constituents. The opium poppy (*Papaver somniferum*), like the marijuana plant, also produces seeds and seed oil with considerable probability of providing nutraceuticals and functional foods. Tobacco (*Nicotiana tabacum*) is proving to be an excellent molecular farm crop, furnishing a variety of medicinally and nutritionally significant materials, especially recombinant proteins of pharmaceutical and nutritional importance. These three species are undergoing development as non-narcotic crops despite the danger they pose from a narcotic perspective and the consequent strong bias against them. Their success has been due to the demand for the beneficial products they have been shown capable of producing, as well as to the fact that they are adapted to temperate areas of the world where substantial investment has been available. The situation is quite different for five popular hot-climate narcotic crops (coca (*Erythroxylum coca*), betel nut (*Areca catechu*), khat (*Catha edulis*), kava (*Piper methysticum*), and peyote (*Lophophora williamsii*)). Their lack of suitability as crops for temperate regions, where the heaviest investment is presently occurring in plant biotechnology and product research, and their apparent lack of alternative, profitable uses, considerably diminishes their prospects of attracting political and investment support. Experience with the marijuana, opium, and tobacco species has shown that they can, with appropriate research and regulation, be used for the benefit of society. Is it not desirable to examine whether other narcotic plants can be converted to production of legitimate products, particularly to assist those in Developing Countries with very limited choices regarding the crops they can profitably grow?

Introduction

SEMANTICS

Several of the key terms used in this presentation are ambiguous (i.e., have more than one meaning) or are vague (i.e., cover a range of meaning). Therefore, some clarification is desirable.

This presentation deals with “narcotic plants,” but the word narcotic is used in different senses. Etymologically, “narcotic” refers to substances that when ingested or otherwise administered induce sleep. In practice, however, narcotics are widely understood to refer to substances that affect the nervous system and may be (1) addictive, (2) harmful, and/or (3) used illegally. Narcotics can have a variety of effects, for example they may be psychotomimetic (mood-altering), psychotropic (mind-altering), and/or hallucinogenic.

The distinctions between medicines and food are somewhat arbitrary. The Greek physician Hippocrates (460?–?377 B.C.), considered to be the father of medicine, is remembered for the saying “Let food be thy medicine.” Plant-based vitamins and a wide variety of chemical constituents in fruits and vegetables provide considerable medicinal benefits (fruits and vegetables *are* medicinal plants, although rarely thought of as such). “Phytomedicines” have been defined as therapeutic agents derived from plants or parts of plants, or preparations made from them, but not isolated chemically pure substances, such as menthol from peppermint. The term “phytonutrient,” which should be used for plant materials that by definition have nutritional value, has been applied to medicinal plant preparations without apparent food value. On the other hand, some substances clearly have both nutritional and medicinal value. In a biological sense, “food” provides needed chemicals that the body can use to produce energy, build or repair tissues, and conduct the complex biochemical transformations that sustain life. However, some plants traditionally considered to be food plants merely deliver high amounts of stimulant chemicals (although almost inevitably plants also provide desirable chemicals such as antioxidants). Such plants include beverages whose chief function is to deliver high amounts of caffeine, such as coffee and tea. Stimulants often have profound effects on dietary habits, and are therefore often nutritionally significant (many of the narcotic plants discussed in this paper are stimulants).

More problematical with the expanding market for herbal components in health foods and preventative medicines are the marketing terms that have developed,

such as “medical foods,” “pharma foods,” and “phytofoods.” The terms “nutraceuticals” and “functional foods” are in the title of this workshop. In September 1996, Canada’s Department of Health (called Health Canada) made available a discussion paper entitled “Recommendations for defining and dealing with functional foods.” This contained the following working definitions: “A functional food is similar in appearance to conventional foods, is consumed as part of a usual diet, and has demonstrated physiological benefits and/or reduces the risk of chronic diseases beyond basic nutritional functions.” “A nutraceutical is a product produced from food but sold in pills, powders (potions) and other medicinal forms not generally associated with food and demonstrated to have a physiological benefit or provide protection against chronic disease.” The term nutraceutical (often spelled nutriceutical in the past) was coined by Dr. Stephen DeFelice of the Foundation for Innovative Medicine, a New Jersey based industry group. His definition was “a food derived from naturally occurring substances which can and should be consumed as part of the daily diet, and which serves to regulate or otherwise affect a particular body process when ingested.” However, the term nutraceutical is now commonly applied to an extremely wide variety of preparations with perceived medicinal value but not necessarily with apparent food value (such as amino acids, essential fats, dietary fibers and fiber-enriched foods, plant and animal pigments, antioxidants, vitamins, minerals, sugar and fat substitutes, fatless meat, skim milk, genetically engineered designer foods, herbal products and processed foods such as cereals, soups and beverages). The phrase “functional food” is also not without controversy. Some have contended that fruits and vegetables should be included in “functional foods” because they are so nutrient-packed, while others would reserve the term for foods fortified in some fashion for health (in this sense, the first functional food seems to have been calcium-fortified orange juice).

However one chooses to make distinctions between food and medicine, it is clear that there is a demand today for foods that are *both* more nutritional and healthy than in the past, and (whether particular health-promoting constituents are consumed separately or combined in food) there is increasing importance attached to “nutritional supplements,” a phrase that nicely summarizes the new trend. Unlike pharmaceuticals, which are usually potentially toxic medications that can only be prescribed by a medical doctor, nutritional supplements for the most part can be purchased from a health food store, herbal practitioner or independent distributor; or they can simply be consumed in fortified foods. Because they are much less expensive than drugs, herbal preparations or extracts, as additions to diet, have been advanced as a new, cost-effective health care system.

The above semantic issues reflect that facts that nature is complex, and terminology is often inexact. However, the focus of this review is straightforward: to examine the extent to which the principal narcotic plants have potential to be developed as sources of nutritional materials, particularly those with marketing potential as nutritional supplements, nutraceuticals, and/or functional food components.

PROBLEMS ASSOCIATED WITH NARCOTIC PLANTS

Most narcotics come from higher (flowering) plants. Although narcotic plants often have considerable medical usefulness, in terms of commercial exploitation they pose three principal problems: (1) they are illegal or at least controlled, so security issues make production and trade both expensive and complicated; (2) considerable stigma is attached to the plants, making it difficult to attract commercial, development interest; and (3) they are highly politicized, with the result that research support is readily available only for projects that are consistent with the prevailing view that the narcotic plant is dangerous and without redeeming values.

REASONS FOR DEVELOPING NARCOTIC PLANTS FOR LEGITIMATE BIOCHEMICALS

Given the above problems, why then should narcotic plants be considered for exploitation as sources of medicinals, nutraceuticals, and functional foods? The reasons are as follows:

(1) All plant species have some unique biochemical characteristics, one never knows which species will be the basis of important scientific and technological developments, and so narcotic plants should not be eliminated a priori from consideration as candidates.

(2) Narcotic plants have a long history of use in medicine, there is no doubt that some chemicals from some species are useful, and the search for additional useful constituents could well be fruitful.

(3) Considerable research has been completed on the biochemistry of narcotic plants, and this knowledge is useful as a basis for further research and development.

(4) The most commonly used narcotic plants are very well understood in terms of their agronomy and processing characteristics. By and large, these species are easy to grow and very productive.

(5) In some cases, industries and peoples have become dependent on income

generated from narcotic plants, and alternative income-generating schemes have not proven successful. Growing the same plants but for legitimate purposes seems like a tactic at least worth considering.

(6) In some cases, varieties of otherwise narcotic species are available that are lacking in the harmful narcotic constituent, or at least are so low that additional breeding could produce "harmless" forms of the plant.

(7) Genetic engineering offers the possibility of complete inactivation of the enzymes responsible for the production of narcotic constituents. Moreover, morphological markers could be added to facilitate identification of such "harmless" forms of narcotic plants.

METHOD OF PRESENTATION

In the following, eight major narcotic plants of the world are reviewed with the specific objective of analyzing their prospects for legitimate exploitation. In each case, background information is first provided, than summary statements are given with respect to the potential for providing medicines, nutraceuticals, and functional foods. Brief mention will be made of their potential as medicinal plants, but since this area is relatively well understood, the focus will be on potential for nutraceuticals and functional foods. First, *Cannabis sativa* will be examined in some detail because, as will be pointed out, it has already achieved notable success in terms of medicinal, nutraceutical, and functional food development, and therefore can serve as a standard of comparison for the other narcotic plants, which are relatively undeveloped. Finally, an analysis will be given of several key considerations that seem to have determined the relative commercial success of *Cannabis sativa*, and the remaining narcotic plants will be examined in the light of these considerations in order to predict the probability of their commercial development.

[Place Figs. 1–4 in the following section, near where they are first mentioned]

Marijuana (Hemp) – *Cannabis sativa* L.

Family: Cannabaceae (hemp family)

Background Information

Cannabis sativa (Fig. 1) is an extraordinary, multipurpose plant. Its stem produces a durable fiber for textiles and many other applications, its flowers provide intoxicating drugs, and its edible seeds are the source of a multi-purpose oil. However, varieties that are useful for producing fiber and oil are quite different from intoxicant varieties, containing far less of the intoxicating chemical tetrahydrocannabinol (THC). This native annual species of Eurasia varies greatly in appearance, depending on variety and how it is cultivated. Plants taller than 6 m have often been recorded, although typically cultivated plants range from 1 to 4 m in height. The sexes are separated on different plants, except for certain cultivated varieties in which male and female flowers occur on the same plant. Male plants are taller, but more delicate in appearance, and they die after shedding their pollen.

Hemp is one of the world's most ancient crop plants, and was valued by the Chinese 8,500 years ago. Historically, the plant was used mostly for fiber. It is one of the oldest sources of textile fiber, and hempen cloth aged 6,000 years has been found. During the age of sailing ships, *Cannabis* was considered to provide the very best canvas, and indeed this word is derived from *Cannabis*. Hemp was introduced to western Asia and Egypt, and subsequently to Europe somewhere between 1000 and 2000 BC. Cultivation in Europe became widespread after 500 AD Hemp was brought to South America in 1545, in Chile, and to North America in Port Royal, Acadia in 1606. It was widely grown in North America until the early part of the present century, followed by a brief revival during World War II. Until the beginning of the 19th century, hemp was the leading cordage fiber. Until the middle of the 19th century, hemp rivaled flax as the chief textile fiber of vegetable origin, and indeed was described as "the king of fiber-bearing plants—the standard by which all other fibers are measured." The majority of all twine, rope, ship sails, rigging and nets up to the late 19th century were made from hemp fiber. Several factors combined to decrease the popularity of hemp in the late 19th and early 20th centuries. Increasing limitation of cheap labor for traditional production in Europe and the New World led to the creation of some mechanical harvesting and processing inventions, but too late to counter growing interest in competitive crops. Development of other natural fibers as well as synthetic fibers increased competition for hemp's uses as a textile fiber and for cordage. Hemp rag had been much used for paper, but the 19th century introduction of the chemical woodpulping process considerably lowered demand for hemp. The demise of the sail diminished the market for canvas. Increasing use of the plant for drugs gave hemp a bad image. All this led to the discontinuation of hemp cultivation in the early and middle parts of the 20th century in much of the world where cheap labor was limited.

Earliest reference to narcotic use of *C. sativa* appears to date to China of 5 millennia ago, but it was in India over the last millennium that narcotic cannabis consumption became more firmly entrenched than anywhere else in the world. Not surprisingly, the most highly domesticated drug strains were selected in India. While *Cannabis* has been extensively used as a narcotic for thousands of years in India, the Near East, parts of Africa, and other Old World areas, such widespread use simply did not develop in temperate countries, where fiber hemp was raised. The use of *Cannabis* as a recreational inebriant in sophisticated, largely urban settings is substantially a 20th century phenomenon. Marijuana, a preparation of leaves and flowers of intoxicant varieties, has become the most widely used illegal drug in the world. (In the past, "marihuana" was the more frequent spelling, but both spellings are correct.) With the exception of alcohol, it is the most widely used recreational drug. At least 25% of North Americans, including 70 million Americans, are believed to have used *Cannabis* illegally. THC, the intoxicating ingredient, is the world's most popular illicit chemical, and indeed the fourth most popular recreational drug, after caffeine, alcohol and nicotine

The use of *Cannabis* for seed oil began at least 3,000 years ago. Until 1800, hemp oil was the most consumed lighting oil in the world. Hemp oil is a drying oil that has occasionally been used in paints and varnishes and in the manufacture of soap.

Hempseed was one of the major grains of ancient China, although there was limited subsequent direct use of hempseed as food by humans. In the past, the seeds were more likely to have been employed as wild bird and poultry feed, than as culinary items. Today, there has been a great resurgence of interest in using hempseed as human food, especially in North America. A principal reason for this is that efficient methods have been found to hull the seeds, i.e. remove the outer hard shell. In the past, hempseed had to be eaten whole, or was only partly hulled, and so was rather gritty. A great difficulty under current regulations in most Western countries is that hempseed has to be sterilized (to prevent plants from being grown from the seed). Once sterilized, the seeds go rancid in a few weeks, unless refrigerated. The oil also goes rancid quickly, unless kept in the dark and refrigerated. Nevertheless, dozens of food items are now currently available in North America, made from hemp seeds. Hemp seeds, oil, and flour are currently being added to many foods. Hemp seeds have an attractive nutty taste, and are now marketed in many forms, often mimicking familiar foods or incorporated into them. Those marketed in North America including nutritional (granola-type) bars, "nut butters," bread, pretzels, tortilla chips, cookies, yogurts, pancakes, porridge, fruit crumble, frozen dessert ("ice

cream"), pasta, burgers, pizza, salt substitute, salad dressings, mayonnaise, "cheese," and beverages ("milk," "lemonade," "beer," "wine," "coffee nog"). The seeds of *Cannabis sativa* do not contain intoxicating constituents. However, if improperly prepared, resin can coat the seeds, and any seed oil that is made from it. In fact, in the past some hemp oils were found to be quite intoxicating.

Medicinal Usage & Potential

Cannabis drug preparations have been employed medicinally in folk medicine since antiquity, and were extensively used in western medicine between the middle of the 19th century and World War II, particularly as a substitute for opiates. Medical use declined with the introduction of synthetic analgesics and sedatives, and there is very limited authorized medical use today, but considerable unauthorized use, including so-called "compassion clubs" dispensing marijuana to gravely ill people, which has led to a momentous societal and scientific debate regarding the wisdom of employing cannabis drugs medically, given the illicit status. There is anecdotal evidence that cannabis drugs are useful for: alleviating nausea, vomiting and anorexia following radiation therapy and chemotherapy; as an appetite stimulant for AIDS patients; for relieving the tremors of multiple sclerosis and epilepsy; and for pain relief, glaucoma, asthma, and other ailments. To date, governmental authorities in the United States, on the advice of medical experts, have consistently rejected the authorization of medical use of cannabis drugs except in a handful of cases. However, in the United Kingdom medicinal marijuana is presently being produced sufficient to supply thousands of patients, and in Canada there is ongoing consideration to supply medicinal marijuana for compassionate dispensation, as well as for a renewed effort at medical evaluation.

Several of the cannabinoids (the unique chemicals in *Cannabis sativa*) are reputed to have medicinal potential: THC (tetrahydrocannabinol) for glaucoma, spasticity from spinal injury or multiple sclerosis, pain, inflammation, insomnia, and asthma; CBD (cannabidiol) for some psychological problems. The Netherlands firm HortaPharm developed strains of *Cannabis* rich in particular cannabinoids. The British firm G.W. Pharmaceuticals acquired proprietary access to these for medicinal purposes, and is developing medicinal marijuana. In Canada, Health Canada has initiated a long-term program of development of medicinal marijuana for research and compassionate use. In the US, NIH (National Institute of Health) has a program of research into medicinal marijuana, and has supplied a handful of individuals for years with maintenance samples for medical usage. Synthetic preparations of THC—dronabinol (Marinol®) and nabilone (Cesamet®)—are permitted in some cases, but are expensive and widely considered to be less effective than simply smoking

preparations of marijuana.

Despite the controversy concerning the medical use of marijuana, increasing efforts are underway to establish the efficacy of specific extracts, and it is possible that these may find accepted usages in modern medicine.

Functional Food Usage & Potential

There are many who believe that the best future prospects for hemp are in the development of the seed oil and its use as a functional food. About half of the world market for hemp oil is currently used for food and food supplements. For edible purposes, hempseed oil is extracted by cold pressing. Quality is improved by using only the first pressing, and minimizing the number of green seeds present. The oil varies in color from off-yellow to dark green. The taste is pleasantly nutty, sometimes with a touch of bitterness. Hemp oil is high in unsaturated fatty acids (of the order of 75%), which can easily oxidize, so it is unsuitable for frying or baking. The high degree of unsaturation is responsible for the extreme sensitivity to oxidative rancidity. The oil has a short shelf life. It should be extracted under nitrogen (to prevent oxidation), protected from light by being kept in dark bottles, and from heat by refrigeration. Addition of anti-oxidants prolongs the longevity of the oil. Steam sterilization of the seeds, often required by law, allows air to penetrate and so stimulates rancidity. Accordingly, sterilized or roasted hemp seeds, and products made from hemp seed that has been subjected to cooking, should be fresh.

The quality of an oil or fat is most importantly determined by its fatty acid composition. Hemp is of high nutritional quality because it contains high amounts of unsaturated fatty acids, mostly oleic acid (C18:1 — 10–16%), linoleic acid (C18:2 — 50–60%), alpha-linolenic acid (C18:3 — 20–25%), and gamma-linolenic acid (C18:3 — 2–5%). Linoleic acid and alpha-linolenic acid are the only two fatty acids that must be ingested and are considered essential to human health. In contrast to shorter-chain and more saturated fatty acids, these essential fatty acids do not serve as energy sources, but as raw materials for cell structure and as precursors for biosynthesis for many of the body’s regulatory biochemicals. While the value of unsaturated fats is generally appreciated, it is much less well known that the North American diet is serious nutritionally unbalanced by an excess of linoleic acid. In hempseed, linoleic and alpha-linolenic occur in a ratio of about 3:1, considered optimal in healthy human adipose tissue, and apparently unique among common plant oils. Gamma-linolenic acid or GLA is another significant component of hemp oil (1–6%, depending on cultivar). GlA is a widely consumed supplement known to affect

vital metabolic roles in humans, ranging from control of inflammation and vascular tone to initiation of contractions during childbirth. GLA is known to alleviate psoriasis, atopic eczema, and mastalgia, and may also befit cardiovascular, psychiatric and immunological disorders. Ageing and pathology (diabetes, hypertension, etc.) may impair GLA metabolism, making supplementation desirable. As many as 15% of the human population may benefit from addition of GLA to their diet. At present, GLA is available in health food shops and pharmacies primarily as soft gelatine capsules of borage or evening primrose oil, but hemp is almost certainly a much more economic source, because it is far easier to cultivate. There are other fatty acids in small concentrations in hemp seed that have some dietary significance, including stearidonic acid. As discussed above, a wide variety of foods made with hempseed and hemp oil are now being sold in North America, and given the health benefits noted above, such fortified foods are in reality “functional foods.”

Nutraceutical Usage & Potential

Hemp oil capsules (Fig. 2) are marketed as dietary supplements (i.e. as nutraceuticals, the benefits of which are discussed above).

Hemp oil has become very significant as a “cosmeceutical” (cosmetic-nutraceutical), i.e. a preparation that promotes the health of skin and allied parts of the body because of the topical absorption of biochemicals. In particular, skin readily absorbs essential fatty acids, so that lotions rich in these substances, like hemp oil as pointed out above, can replenish cells damaged by sun and dry air. For this reason the Body Shop, a well known international chain of hair and body care retailers, introduced a wide variety of lotions and cosmetics made with hempseed extracts (Fig. 3). In 2000, the Body Shop reported gross sales of about a billion dollars annually, with about 4% of sales constituting hemp products. Hemp oil is now marketed throughout the world in a range of body care products, including soaps, shampoos, bubble baths, perfumes, creams, lotions, moisturizers, and lip balms. Hemp-based cosmetics and personal care products account for about half of the world market for hemp oil.

Summary Assessment

Cannabis sativa is currently being used as a source of medicinal, nutraceutical, and functional food constituents, despite the fact that it is the world’s most widely used narcotic plant. It therefore provides a model of how other narcotic plants might potentially be similarly developed. There are several reasons why *C. sativa* has been

successfully developed. First in importance is the fact that varieties useful for producing nutraceutical and functional food constituents are very low in the narcotic constituent, and so have limited potential for abuse. This has persuaded the authorities in many countries that cultivation of these varieties should be permitted. Second, *C. sativa* is extraordinarily versatile in the range of products that it can furnish (note Fig. 4), and this flexibility has made it attractive as a crop, which in turn has increased the volume of material available, and reduced costs. Third, with particular reference to medicinal aspects, the stigma that is attached to marijuana is not as severe as has been attached to some other narcotics, and the idea that this "soft" narcotic could be used as a medicine has seemed attractive to many simply because they approve of the drug.

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[Place Fig. 5 in the following section]

Opium Poppy (Oil Poppy) – *Papaver somniferum* L.

Family: Papaveraceae (poppy family)

Background Information

The opium poppy (Fig. 5) is an annual, growing as high as 2 m, with attractive white, pink, red, bluish or purple flowers (doubled in some garden forms, i.e. with extra petals) to 10 cm across. The species is believed to grow wild in the Mediterranean region, from the Canary Isles eastwards. It is found as an escape from cultivation in fields, roadsides, and waste places in scattered localities throughout North America. The opium poppy has been selected to produce three kinds of plants: narcotic cultivars, oilseed/condiment cultivars, and ornamentals. Virtually all varieties of opium poppy have some opiate drugs, so the cultivation of the plants, either for food or for legitimate drugs, is strictly controlled. The culture of the opium poppy is against the law in North America, even as a garden ornamental. Nevertheless, opium poppy persists in old gardens and around abandoned homesteads in North America, and is occasionally planted, innocently or not. Most people are unaware that the source of poppy seeds commonly used on bakery products is the opium poppy, exactly the same species that produces opiate drugs such as heroin. Indeed, the very same plants are often the source of both products.

Crude opium is the hardened milky sap of the unripe fruit. Dried latex is obtained from unripe capsules, and is used medicinally as well as for illicit narcotics. The drug opium is a mixture of many constituents, including the alkaloids morphine and codeine. It has traditionally been obtained by making incisions into the nearly ripe poppy capsules 10–20 days after flowering. In cooler climates incisions do not seem to result in good exudation of latex, and mature capsules are simply collected for chemical extraction. Morphine is often extracted from the capsules of oilseed cultivars after the seeds have been harvested, although narcotic cultivars are more productive. Heroin is manufactured from morphine. The major illegal growing areas are: in the highlands of mainland Southeast Asia (especially Burma, Laos, Thailand, and adjacent southern China and northwestern Vietnam); in Southwest Asia (notably Pakistan, Iran, and Afghanistan); in Mexico; and to a lesser extent in Lebanon, Guatemala and Columbia.

The narcotic effects may have been known to the ancient Sumerians, about 4000 BC, as they had a symbol for it that has been translated as “joy plant.” The opium poppy was well established in classical times. It was familiar to ancient Egyptian, Greek, and Roman civilizations, and seems to have been used effectively as a therapeutic drug. However, by the time of Mohammed (570–632) the narcotic qualities were also appreciated in Arabia. Islamic traders and missionaries spread the cultivation of the opium poppy to Persia, India, China, and Southeast Asia, where it

was used to relieve pain, but also began to be used excessively as a habit-forming, destructive narcotic, initially in India, then in China. The drug was first eaten in the Orient, but began to be smoked in the 17th century in China, which resulted in a tremendous upsurge of use and production. Crude opium has a disagreeable smell and a hot biting taste. The Swiss alchemist Paracelsus (1493–1541) overcame these objectionable features by making up a solution of opium in alcohol. This deadly mixture, known as tincture of opium or laudanum, enslaved numerous people during the following centuries. Portuguese, Dutch, and British merchants trafficked extensively in opium. In the 19th century, the British brought about the Opium Wars of 1840 and 1855 to prevent the Chinese from outlawing the opium trade. It has been estimated that in 1886 about a fourth of the Chinese (approximately 15 million people) were addicted to opium. During Victorian times in England, tincture of opium was readily available, and was often administered to teething or upset babies to make then sleep. In the United States, opium preparations became widely available in the 19th century, and morphine was used so widely as a painkiller for wounded soldiers during the American Civil War that opium addiction became known as “the army disease” and “soldier’s disease.”

The economic part of the plant for culinary purposes is the seed. The kidney-shaped seeds range through white and yellow to slate-blue or black, and are tiny. They and the oil expressed from them have essentially no narcotic properties. In mature wild plants the wind shakes the seeds out of the fruit through pores at the apex. Like the narcotic use, The culinary use of the opium poppy is ancient. Many seeds have been found at the sites of ancient domiciles, including Swiss Lake Dwellings of Neolithic Age (at least 4,000 years ago). About 2000 BC the Egyptians cultivated poppy to obtain the edible oil in the seeds. The Classical Greeks also used poppy seeds as a food. Both the ancient Greeks and Romans added the seeds to cakes and bread as a flavoring. By the Middle Ages, the use of poppy seeds as a condiment on bread was well established. Today, poppy seed is legally produced in the Netherlands, Poland, Romania, the Czech Republic, the former Yugoslavia, Russia, India, Iran, Turkey, Argentina, and many Asian and Central and South American countries. Most importation to North America is from Australia and The Netherlands.

Forty to 60% of the weight of opium poppy seeds is oil, and the plant is commonly grown as a source of edible and industrial oil. Poppy oil is a pale yellow, fixed, tasteless, oil, useful as a salad oil as it is less liable to become rancid than olive oil. The oil is also used to make margarine and salad dressing, and is employed as a cooking oil. In southern Europe poppy seed oil is not competitive with olive oil, and so is not produced. Artists use poppy seed oil as a drying oil, useful in paints and

varnishes. The oil is also a component of some soaps.

Medicinal Usage & Potential

The opium poppy is the source of important pharmaceutical alkaloids. Morphine and codeine are widely used as analgesics and cough suppressants. Codeine is a constituent of over 22% of analgesic preparations in the United States. Papaverine is a vasodilator and smooth muscle relaxant. Sanguinarine is antimicrobial and anti-inflammatory. Noscapine is antitussive and anti-tumorogenic. Opium poppy has been used as a tranquillizer and analgesic for millennia. It has also been employed as an aphrodisiac, and to treat numerous medical conditions, and continues to be used in China for a variety of medicinal purposes. Centuries of abuse of the drug as a recreational inebriant, and the well known misery that has resulted, suggest that the opium poppy has been more of a curse on humanity than a blessing. However, opium poppy is one of the most important medicinal plants, and scarcely anyone has not experienced pain relief by taking medically prescribed morphine or codeine.

Much of the poppy grown for the extraction of opium for medicinal purposes is cultivated in government-regulated farms in India, Turkey, and Tasmania (Australia). Limited authorized pharmaceutical production also occurs in Europe. Growing poppies for pharmaceuticals in North America is also possible under license, but insignificant production occurs.

Functional Food Usage & Potential

Poppy seed meal left after pressing oil from the seeds is a good source of quality protein, which can potentially be used in the preparation of functional foods.

Nutraceutical Usage & Potential

Poppy oil is rich in the unsaturated oleic and linoleic acids, and therefore like *Cannabis sativa* described above, is potentially useful as a source of nutritional supplements.

Summary Assessment

The opium poppy is already an established medicinal and culinary plant. Within the last decade, low-morphine forms have been found, and these may serve as the basis for cultivars that can be grown with reduced security costs. Extracts from poppy seeds can be used for nutraceuticals and functional foods, but breeding of

suitable cultivars is necessary, and it is uncertain whether opium poppy can be competitive in these product areas. The species is quite productive, and the probability is that it can be developed as a commercial source of nutritional supplements.

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[Place Figs. 6 & 7 in the following section]

Coca (Cocaine Plant) – *Erythroxylum* species (especially *E. coca* Lam. and *E. novogranatense* (D. Morris) Hieron.)

Family: Erythroxylaceae (coca family)

Background Information

In the words of the late Richard Evans Schultes (1979), a renowned expert on hallucinogenic plants, “Coca must be rated as the most important and culturally significant narcotic of South America. It likewise is the psychoactive plant that, of the New World flora, has played the greatest role in Western medicine.”

Erythroxylum is widely but incorrectly spelled *Erythroxylon*. The species are known as coca. Coca is widely confused with cacao (*Theobroma cacao* L.), the source of chocolate.

Erythroxylum coca (Fig. 6) is most often known simply as coca. It is also

called cocaine plant and spadic. Two varieties have been recognized. *Erythroxylum coca* var. *coca* is called Bolivian coca and Huanuco coca and is widely cultivated in South America. *Erythroxylum coca* var. *ipadu* Plowman is called Amazonian coca and is cultivated in Amazonian Colombia, Peru and Brazil.

Erythroxylum novogranatense is also generally called coca, and also has two varieties. *Erythroxylum novogranatense* var. *novogranatense* is called Colombian coca, and is cultivated in Colombia and Venezuela. *Erythroxylum novogranatense* var. *truxillense* (Rusby) Plowman is called Truxillo coca and Trujillo coca. It is cultivated in southwestern Colombia, Ecuador, and northern Peru.

Coca plants are small evergreen shrubs with reddish brown bark. *Erythroxylum coca* is the major source of commercially produced coca leaves and cocaine. It is 2–4 m in height, but usually kept no higher than 2 m when cultivated. The leaves are 3–5 cm long, and resemble bay and tea leaves. The foliage contain 0.1 to1% cocaine, with higher amounts tending to occur at higher altitudes. The species is native to fertile warm valleys under 2,000 m in the tropical region of the eastern Andes Mountains, and is widely cultivated in South America. *Erythroxylum novogranatense* is closely related to *E. coca*, but is considerably less important. It is grown mostly in Colombia and Venezuela, and also in northern Peru and Brazil.

Why do coca plants produce cocaine? Cocaine is a natural pesticide defence, which acts to poison the nervous systems of many insects which try to feed on the plants.

South American Indians have cultivated coca plants for thousands of years (note Fig. 7) for use as a masticatory (a substance that is chewed). Ceramic figurines from Ecuador of 3000 BC show men with the bulging cheeks characteristic of the coca chewer. Coca was used from Nicaragua in the north down to Chile in the south, generally only by the elite, including Royalty and the ruling classes. Coca was especially employed in religious rituals and, after the Spanish conquest of South America, the Catholic Church condemned the use of coca, viewing its use as a heathen exercise in spiritual life. The Spanish, however, realized that coca remarkably increased the stamina of workers, and encouraged the cultivation of coca to supply their slaves in the rich silver and tin mines of Bolivia. By the late 1800s Europeans and North Americans were aware of the stimulant reputation of coca, and were using it in elixirs and patent medicines. The most infamous use of the coca plant was in the popular soft drink Coca-Cola. (This did not become completely cocaine-free until 1929. In modern times, de-cocainized coca leaves have been used for flavoring.) Today, millions of Indian in the Andes and in the western Amazon

continue to chew coca leaf. Although Peru, Bolivia and Colombia are the major producing countries, coca is now cultivated outside of South America, particularly in Africa, Ceylon, Taiwan, and Indonesia. Colombia alone is responsible for two-thirds of global coca leaf production.

Coca leaves are dried, and may be powdered for use. When chewed or (more often) sucked with a pinch of lime, coca leaf releases alkaloids, principally cocaine, which exerts a stimulant action. The effect from the small amount of cocaine in the leaves is very much milder than exposure to refined cocaine. Coca leaves do not produce the strong euphoria associated with the abuse of cocaine. There is a numbing of sensory nerves and a dulling of hunger and pain. The Indians used coca leaves to acquire strength, endurance, and increased stress tolerance to hunger and cold. Chalk or ash is usually added to increase the alkalinity and dissolve the alkaloids into the saliva. Lime decreases the acidity in the mouth, and this makes the alkaloid more available. The practice of using lime to make alkaloids more available is widely practised by different cultures using different plants (the same is done, for example, with betelnut, described below).

In the South American Andes, peasants have traditionally sucked wads of leaves, keeping them in their cheeks for hours. Studies have shown that chewing or sucking 100 g of coca leaves satisfies the daily dietary allowance for calcium, iron, phosphorus, and vitamins A, B, B_2, and E. This contribution of vitamins has been shown to be desirable in the starch-heavy diet of the highland South American Indians.

Today, the illegal marketing of refined cocaine is an extremely serious social, health, and law enforcement problem. Importation and production of cocaine have been controlled by enormously powerful armed cartels such as the Medellín and Cali cartels in Colombia, which have infiltrated governments, corrupted officials, and assassinated public officials. The yearly US retail cocaine market has been estimated to be worth between $30 billion and $150 billion. Bolivia’s yearly income from cocaine exports has been estimated to be about a trillion dollars. North American cocaine dealers make ten times more than the Bolivian producers do. The peasants who grow the coca receive less than 1.5% of the value for which cocaine is sold in the United States.

The United Nations Convention Against Illicit Traffic in Narcotic Drugs and Psychotropic Substances, signed in Vienna in 1988, prohibits sowing, cultivating, harvesting, processing and marketing of coca leaves. In most countries, possession of coca leaves could lead to arrest and prosecution. The traditional usage of coca leaf in

South America represents a cultural heritage that does not deserve the condemnation that properly is assigned to the abuse of cocaine. Unfortunately, and not for the first time, the priorities of South America's indigenous peoples are taking second place to those of foreigners. As part of the "War on Drugs," huge efforts and expenditures are underway to eradicate coca plantations, and there are well-intentioned crusades to encourage the planting of replacement crops, which are not as attractive to peasants in extreme poverty.

Medicinal Usage & Potential

Coca leaf has a long history of use as a medicinal plant in South America, and cocaine has been used in Western medicine. Cocaine was well regarded in the late 19th century. Its use was advocated by such prominent public figures as Pope Leo XII, Sigmund Freud, Jules Verne, and Thomas Edison. Cocaine has been observed to be effective against eczema and shingles (herpes zoster), and as a bactericide against gram-negative bacteria. It has been used as a local topical and as a spinal anesthetic. However, synthetic anesthetics such as procaine are now used. In the 19th century, cocaine was used as a "cure" for morphine addiction. However, cocaine is extraordinarily addictive; starving experimental animals have been observed to choose cocaine in preference to food.

Functional Food Usage & Potential

In a sense, coca plants are currently used to prepare a kind of functional food (although not actually contributing nutritional value). In Peru and Bolivia, tea made from the coca leaf is widely available. Public markets not only sell loose coca leaves, but grocery stores often provide commercial tea bags made with coca. Restaurants in these countries also offer hot coca ("maté de coca"), a clear tea similar to green Asian tea, but with less color and flavor. Hotels and airports commonly offer complementary coca tea to tourists, who are often informed that the beverage will counter the fatiguing effects of altitude. Most tourists who try coca tea report that they experienced no obvious effects. During a 1993 visit to Bolivia, Pope John Paul II (1920–) is said to have consented to drink coca tea, a mark of respect for the culture of the indigenous population.

Nutraceutical Usage & Potential

No uses were found.

Summary Assessment

Coca leaves function as a stimulant, and under the time-tested conditions of consumption by South American aboriginals, such usage is advantageous. In theory, stimulant beverages could be manufactured, based on the coca plant, but given the curious history of how cocaine was once present in Coca-Cola, such use seems unlikely to be resurrected. Although other alkaloids have been implicated, cocaine is the chief contributor to the stimulant effect. To date, the plants have not been shown to be useful sources of other components that could be employed as nutritional supplements. Given the current notoriety of cocaine, it is therefore highly improbable that coca plants can be used for nutraceuticals or functional foods.

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[Place Figs. 8 & 9 in the following section, near where first mentioned]

Betelnut (Arecanut) – *Areca catechu* L.

Family: Palmae (Arecaceae; palm family)

Background Information

The betel palm (Fig. 8) is a tropical, Asian tree with a slender trunk typically 12–15 m, sometimes up to 30 m tall, and about 50 cm wide, green at first, then greyish and ringed by the remains of scars where the old leaves were attached. The fruits are generally the size and shape of small (hen's) eggs, up to 5 cm in diameter, hard, red-orange, yellow or scarlet, with a fibrous layer under the shell. A betel palm may produce up to 250 fruits annually. Each fruit contains one acorn-shaped (nearly round) seed about 2.5 cm in diameter, which is brown with fawn marbling. The seed is called "betel nut," and contains arecoline, an alkaloid chemical, which is responsible for a narcotic/stimulant effect. Also present are tannins, which are responsible for astringency (producing a mouth-puckering effect), and a red dye that results in red spittle, red lips, and red feces. Laborers chew betel to provide them with energy, and betel has played much the same role where it is common as coffee and cigarettes do in the West. The species is cultivated in the Old World tropics. Its native range is obscure, possibly the East Indies and Malaysia. This palm is widely cultivated, and there are huge plantations in Asia from Pakistan and India to Malaysia, extending as far as the Pacific Southern Islands, and also in Africa. Betel palm is sometimes grown as an ornamental in subtropical southern Florida, and can also be cultivated in some of the warmest parts of California. There is considerable commerce in betel nuts, which are mostly used in India, Southeast Asia, Malaysia, and Polynesia, but are also imported into North America.

Betel nuts are traditionally consumed with "betel leaf," which is obtained from the betel pepper, *Piper betle* L. (Fig. 9). This species is also known as betel and betelvine. It probably originated in Malesia, and is cultivated along with betel palm in the Old World tropics. It is a herbaceous, evergreen, red-berried plant, the stems extending as far as 5 m. The betel pepper is widely cultivated in southern Asia, where betel has been chewed since ancient times. Betel pepper leaves can not be imported into the United States.

"Betel" is a traditional, mild, legal, narcotic stimulant of Asia which, as explained below, is made by combining the seeds of the betelnut palm, the leaves of the betel pepper, and other ingredients. Chewing betel is widespread in South-East Asia and the South Pacific islands and among those of Indian origin elsewhere in the world. It is estimated that about 500 million people chew betel. Betel chewing is an ancient habit, that may have originated in India. The 13th century traveller Marco Polo mentioned in his diaries that Indians were in the habit of consuming betel.

Spitting out the red juice that is generated, as well as the remaining pulpy mass, is generally considered disgusting in Western countries. Naive Westerners have sometimes interpreted the spectacle as spitting blood, as was once common in people with tuberculosis. Nevertheless, this behavior has been accepted where betel consumption is practised. However, in some areas of Asia the staining of roads and walls of public buildings, as well as health concerns, has led to a growing social disapproval of betel. Even where betel chewing is permitted, it is often banned in certain public places, such as airports. While it is difficult for those not familiar with betel chewing to understand its attraction, it is in principle no different from coffee consumption.

Arecoline from the betel nut is considered to be chiefly responsible for the stimulant effect of betel (arecoline is converted by the central nervous system to the stimulant arecaidine). Arecoline is released from the nut by saliva and lime. This chemical is in the same alkaloid group as muscarine, found in fly agaric (preparations of the fly agaric mushroom used to be widely used left open in dishes to kill flies, and are still used as a pyschedelic). Arecoline is the fourth most popular legal natural stimulant drug, after caffeine, alcohol, and nicotine, in that order. On the basis that they contain “a poisonous or deleterious substance,” primarily arecoline, betel nuts were outlawed in the United States in 1992, although the ban was partially lifted in 2000.

Lime is calcium oxide. “Burnt” or “slaked” lime (hydrated calcium oxide, calcium hydroxide) is preferable, and is often prepared by burning seashells or coral. The addition of lime makes the betel mixture alkaline, and this in turn causes the arecoline (and additional alkaloids that are present) to be absorbed in the mouth more readily. Catechu, a wood preparation that is also sometimes added, presumably has the same effect. If lime is omitted from the chew, the characteristic effect is almost absent.

Just why betel leaf (from *Piper betle*) is traditionally combined with betel nut (*Areca catechu*) isn’t entirely clear. Certainly the aromatic leaf improves the taste, and is responsible for the commonly reported sweet taste and pleasant breath that results. The leaf also counters the burning, astringent taste of the betel nut, and may promote the nut’s physiological effect.

There is evidence that the habit of chewing betel containing tobacco, which is frequently added to the quid, is carcinogenic in humans (but see below). There is suspicion that chewing betel without tobacco is also carcinogenic in humans, and it has been suggested that betel consumption is linked to heart disease, diabetes, and

asthma. An overdose of betel can cause dizziness, vomiting, and convulsions. The use of betel has decreased dramatically over the last half century and has been replaced by tobacco, hardly an improvement since lung cancer has increased.

Betelnut and some other intoxicants are far more popular in Asia than in Western nations, and by contrast high-alcohol, distilled beverages are far less popular. This difference in popularity of inebriants has been credited in part to the low levels of aldehyde dehydrogenase isozyme in Asian peoples, an enzyme in the liver that helps to metabolize alcohol.

Medicinal Usage & Potential

Betelnuts have been employed in Asia for a variety of traditional medicinal applications, particularly as an anti-helminthic.

In 2004, a British patent application was announced for a betelnut and nicotine chewing gum. The gum is intended to be used in assisting tobacco users to escape their addiction, although the combination of two addictive substances seems contradictory for the purpose. However, betelnut has been found to be anti-carcinogenic against tobacco (Padma et al. 1989).

Functional Food Usage & Potential

No usages have been identified.

Nutraceutical Usage & Potential

Several reports (Padmaja et al. 1994; Loo and Choi 1999*a*, 1999*b*) have indicated that betel constituents have beneficial effects on skin, suggesting the possible use in cosmeceuticals.

A very minor oral use of betel in Asia is as a dentifrice. The nut is burned to make a charcoal, which is pulverized and added to toothpaste. Likely the betel alkaloids have a minor antibacterial effect.

Summary Assessment

Although declining, betelnut cultivation remains extremely widespread. Although increasing in social disfavor, betelnut remains a permitted social stimulant in most countries, and the degree of disapproval is far less than for most narcotics. The betelnut is a tree and, unlike annual crops, reducing the size of the crop can only

occur slowly. These considerations mean that there will be a large supply of betelnuts for the foreseeable future, and that these are potentially available for the development of pharmaceuticals and nutritional supplements in the future. This would seem to be an example of a narcotic plant that deserves research investment in order to identify and develop constituents as marketable products.

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[Place Fig. 10 in the following section]

Khat – *Catha edulis* (Vahl) Forssk. ex Endl.

Family: Celastraceae (staff-tree family)

Background Information

Khat (Fig. 10) is an evergreen shrub or tree, mostly growing 2–7 m in height, occasionally to 15 m, rarely to 25 m. It is usually cut back in cultivation to form a shrub, making it easier to harvest the twigs and leaves, the economically important parts of the plant. The leaves and sometimes also the young twigs are consumed as a masticatory for a stimulant effect. The leaves are up to 10 cm long, resemble those of basil, and emit a strong, sweetish smell. They are crimson-brown and glossy when young, becoming yellow-green and leathery as they age. The young branches near the top of the plant produce the best material, but the middle and lower leaves and stems are also used. In wetter regions khat shoots are tender and the soft green twigs are also consumed. In dryer regions the twigs are woody and bitter, and only the leaves are used. The youngest leaves are usually quite weak in narcotic effect in comparison to the more mature ones. At the retail level, khat is sold in leafy bundles, wrapped in banana leaves or plastic to preserve freshness. Each bundle contains the quantity of leaves and stem tips that most consumers chew in 1 day.

The species is native to northeastern Africa, and was probably domesticated in the Ethiopian highlands, although some have suggested an independent domestication in Yemen. Khat is cultivated primarily in countries in East Africa and the Arabian peninsula. In Yemen, it has been estimated that more than half of the arable land is now used to cultivate khat, which has replaced other crops, particularly coffee. Khat is Ethiopia's second largest crop, after coffee. It is also grown in Kenya, Somaliland, Tanzania, Madagascar, and Uganda. Ethiopia and Kenya are principal exporters. The taste for khat is acquired, and is almost completely restricted to people who have been culturally habituated to it. Khat is consumed in many Old World countries, including Kenya, Malawi, Uganda, Tanzania, Arabia, the Congo, Zimbabwe, Zambia, Madagascar, South Africa, Somalia, Ethiopia, and Yemen. The species is also grown as an ornamental in warm areas, such as Florida and California.

Khat is mostly used by males in friendly social situations, typically consumed during most of the evening and night. The harvesting, dealing, and sorting were traditionally almost entirely left to women. In more recent times, women have taken up holding their own sessions, separately from the men. In the Old World, depending on the country, 10 to over 60% of women now consume khat. In Yemen, it has been reported that women's sessions typically have dancing and music, and are often more lively than men's meetings. On a world basis, it has been estimated that 5 to 10 million people use khat, consuming about 5 million kg (11 million pounds) of leaf material daily.

Khat chewing is generally believed to have originated and spread from Yemen. A study of ancient Egyptian hieroglyphics has suggested that khat was used for ritual religious purposes. Khat has certainly been used at least since the 13th century as a recreational and religious drug in Eastern Africa, the Arabian Peninsula, and throughout the Middle East. It is traditionally consumed in many Muslim countries where alcohol is forbidden by religious law. However, until the late 1970s, khat chewing was largely a weekend habit of the rich. More recently, khat was taken up by a large proportion of Yemen's population (over 90% of the male adults), as well as by many in Ethiopia, Somalia, and Djibouti.

During the 1980s, a flood of refugees from the horn of Africa entered the United States, Canada, Australia, and various West European countries, and brought with them their custom of chewing khat. As the leaves become old or dry, their stimulatory ability is reduced. Because only fresh khat has a strong effect, fresh material has often been transported into many countries by plane, especially for emigrants to Britain and North America habituated to its use. Because khat in leaf form starts to lose its potency after 48 hours, it is frequently shipped to North America on Thursdays, Fridays, and Saturdays for weekend use. In North America, the use of khat is most popular among immigrants from Yemen and the East African nations of Somalia and Ethiopia.

The stimulating ability of khat is due mostly to the alkaloid cathinone, which is closely related to and as potent as amphetamine. Cathine, a milder form of cathinone, is also present. Cathinone, the most potent active principle of khat, is chemically unstable; it has a half-life potency of only 1½ hours, and 2–3 days after harvest cathine is the only significant stimulant remaining, explaining why khat users prefer to chew only fresh leaves and shoots. (Deep-freezing has been reported to prolong the potency of khat for months.) When chewed in moderation, khat alleviates fatigue (or increases energy), reduces appetite, and increases alertness. About 30% of users have reported becoming sleepy rather than excited. Self-esteem and the ability to communicate are usually increased, typically taking the form of users embarking on long speeches in the belief that they are treating their listeners to pearls of knowledge.

Khat is exceptionally high in ascorbic acid (vitamin C), and the practice of chewing it is believed to supply users with some of their daily requirements. Curiously, ascorbic acid has been reported to act as an antidote to amphetamine-like substances such as are present in khat.

Khat users can develop ill effects similar to those associated with

amphetamines, including mental or emotional problems such as increased irritability, aggression, depression, anxiety, and paranoid delusions. Frequent use may be associated with loss of appetite, digestive difficulties, cancer of the mouth, heart disease, and loss of sexual potency. Where khat use is prevalent, it has been claimed that the semi-drugged condition of many workers slows economic production. Khat is usually not considered a physically addictive drug, but in 1973, the World Health Organization listed it as a "dependence producing drug," i.e. one for which a strong craving has developed.

Although the use of khat is predominantly by Muslims, less than half of one percent of the world's Muslims use the drug. Although Muslim religious leaders are divided on whether or not the use of khat contravene's the Koran's general injunction against the use of intoxicants, the World Islamic Conference for the Campaign Against Alcohol and Drugs, which met at Medina, Saudi Arabia in May, 1983, issued the following resolution:

> "After reviewing reports submitted to the Conference on the health, psychological, ethical, behavioral, social and economic damages resulting from khat, the Conference judges khat to be a drug prohibited by religion and accordingly the Conference recommends to Islamic states to apply punishment of the basis of Islamic Shari'ah [canon law] against any person who plants this tree and markets or consumes khat."

Most Arab countries have outlawed khat. The Ethiopian and Somali governments have

prohibited khat by law, but in practice this has not reduced consumption or production. Fresh khat is also illegal and classified as a narcotic in the United States, Canada, and much of Europe, although most of this prohibition is quite recent. Although khat often is still smuggled in, due to the cost (often 25–50 dollars for an evening's supply for one person) many immigrants habituated to khat have turned to beer, which is cheaper and more available. As with other strongly desired drugs that society has made illegal, a Mafia-like control has developed over production and distribution.

A 1973 estimate suggested that over 4 billion hours of work a year were lost in Yemen as a result of khat chewing and, whether true or not, khat has a reputation for encouraging laziness. In 1967, the Marxist government of South Yemen attempted to do away with khat because of this belief. With wide resistance to a total ban, the government imposed a heavy tax. Surprisingly, the people paid the tax and

kept on chewing. By 1985 khat ranked first among taxes on agricultural products and second among all excise duties in increasing revenue. A 1992 report of the Yemen Times suggested that the value of khat to the Yemeni economy was twice the value from cultivation of all other crops. The World Bank has estimated that an astounding one-quarter of the national income of Yemen is spent on khat.

Medicinal Usage & Potential

Khat is not used medicinally in modern medicine.

Functional Food Usage & Potential

A khat-based frozen concentrate, "Pisgat," is manufactured and sold in Israel as a health food, its maker claiming that 2 tablespoons is equivalent to the effect achieved by several hours of chewing fresh khat.

Nutraceutical Usage & Potential

No uses were found.

Summary Assessment

Khat usage is mostly associated with poor people living in Developing Countries. There is no doubt that the effects of khat have been entirely negative. Unfortunately this is an example of a situation that is not attractive for investment and research from well-off countries. Without such investment, the prospects for discovering and marketing nutritional supplements and pharmaceuticals from khat are very limited. Investment is particularly discouraged because of (1) the dependence on the wild supply (such dependence is often uncertain in arid climates and politically fragile countries); and (2) the very negative public image of khat.

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[Place Fig. 11 in the following section]

Kava (Kava-Kava) – *Piper methysticum* G. Forst.

Family: Piperaceae (pepper family)

Background Information

Kava (Fig. 11) is a shrub, generally about 2 m tall, but in favorable circumstances it grows as high as 6 m. There are separate male and female plants, but the females tend to be sterile (unable to produce seeds) and as male plants are common, the species is usually propagated vegetatively. The stems are green to black, succulent, with strongly swollen nodes reminiscent of bamboo stems. The leaves are heart shaped, 15–28 cm long, and when held up to light appear dotted because of the presence of oil-containing glands. The species is thought to have originated in Melanesia and is common in Polynesia. Kava is believed to have been cultivated on islands in the South Pacific for over 3,000 years. A drink made from the kava plant was the beverage of choice for the royal families of the South Pacific, and indeed kava has been called “the South Pacific’s most revered herb.” The first Europeans to observe the plant and its ritualistic consumption by natives of Oceania were Dutch explorers Jacob Le Maire and William Schouten in 1616. It was noted that natives chewed or pounded the rhizome (underground stem, usually called a “root”) and

mixed it with water to produce a brownish, often bitter brew which they then consumed for its psychoactive properties. Kava's active chemical are called kavalactones, and are concentrated in the "roots." The drink is still consumed in Western Polynesia, especially in Samoa, Tonga, and most of Melanesia including Fiji, although missionaries reduced its use considerably. Kava was also traditionally employed as a medicine for various ailments, and has been used as a sedative and aphrodisiac.

While kava is sometimes considered to be a "drug," it is more properly viewed as a traditional social beverage, much like wine. Indeed, in many of the Oceanic islands where kava was used, alcoholic beverages were unknown. As with alcoholic beverages, heavy consumption of kava can cause intoxication and loss of coordination. Many procedures have been used to prepare kava traditionally. In the "Tonga method," the rhizome is chewed by young men or women until it is fine and fibrous, then soaked in water, and after a period of time decanted and drunk. In the "Fiji method," which is currently the most widespread, the rhizome is first mechanically pulverized, followed by the extraction of the residue with water.

At least until recently in modern times, the "narcotic" image of kava has been very minor, as evidenced by the following. Former First Ladies Claudia "Lady Bird" Johnson (1912– , wife of the 36th president, Lyndon Baines Johnson) and Hillary Rodham Clinton (1947– , wife of the 42nd president, William Jefferson Clinton), and Pope John Paul II (1920–) drank kava during welcoming ceremonies in the Pacific, respectively in 1966, 1992, and 1986. Queen Elizabeth II (1926–) of Great Britain and members of the Royal Family have consumed kava during visits to Fiji on a number of occasions.

Medicinal Usage & Potential

Among herbal supplements, kava ranked ninth in sales at the beginning of the 21st century in the United States, so that is almost entirely in this form that North Americans are consuming the plant. Some information on the effects of it are therefore in order. When drunk or eaten in its paste form, the tongue and inside of the mouth go numb, as with a shot of novocaine. However, commercial preparations (tablets, capsules, extracts, tinctures, drinks, and tea bags) are usually diluted to prevent this. Kava reduces anxiety much like the well known Valium, and is a potent muscle relaxant. It promotes relaxation and sociability, but its effects are different from those produced by either alcohol or synthetic tranquillizers. It does not result in a hangover, and, even more significant, it does not cause dependency or addiction. Not surprisingly, in recent times kava has become extremely popular, and has been

widely marketed specifically to reduce anxiety, depression, and insomnia.

In 2002, the US Food and Drug Administration cautioned that there is potential risk of severe liver injury from the use of dietary supplements containing kava. Recent reports from health authorities in Germany, Switzerland, France, and the United Kingdom linked kava use to at least 25 cases of liver toxicity, including hepatitis, cirrhosis, and liver failure. Canada banned kava in 2002. Kava products are also banned in Germany and Singapore, and some countries have also either banned the sale of kava or taken measures to restrict the market. It has been noted that liver damage appears to be rare. Those with liver disease or liver problems, or taking drugs that can affect the liver, should discuss the problem with their health care practitioner before using kava. Kava should not be consumed along with alcohol. Use of kava is discouraged during pregnancy and breast feeding, and by those with Parkinson's or clinical depression. Children should not be given kava. Prolonged use can result in yellow coloration of skin, nails, and hair, allergic skin reactions, and visual and equilibrium disturbances. In Europe it has been recommended that kava not be consumed for longer than 3 months without medical advice, and that driving and operating machinery during consumption should be avoided.

Functional Food Usage & Potential

As noted above, kava has been classified as a "dietary supplement," although in fact it is used as a tranquilizer. Although added to a variety of beverages, it really can not be considered to be a functional food component.

Nutraceutical Usage & Potential

No uses were found.

Summary Assessment

Kava is an example of a mild narcotic that has achieved considerable market penetration until health concerns were raised recently. Its success, as with other herbal tranquillizers, is due to a combination of the demand for natural (botanical) stress relaxers in modern times, the effectiveness of the drug constituents, and the rather attractive image of the plant's use as an ethnic inebriant. Kava has not been used significantly as a food plant, at least for nutritional purposes, and does not seem particularly useful for development as a source of nutritional materials.

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[Place Fig. 12 in the following section]

Peyote – *Lophophora williamsii* (Lem. ex Salm-Dyck) J.M. Coult.

Family: Cactaceae (cactus family)

Background Information

Peyote (Fig. 12)is a small, dome-shaped, light blue-green cactus. Unlike most cacti, the plant is spineless, although spines are present in very young seedlings. Most of the plant is underground, in the shape of a taproot similar to a large carrot. Only a short stem (the “button”) occurs above ground. The button is 2–7 cm high, and 4–12 cm in diameter. The plant has pink flowers 1–2.4 cm long, which develop at the densely wooly top of the button, and turn into fruits that are 15–20 mm long, fleshy and pink or red at first, maturing to brownish white and dry at maturity. Peyote grows as single plants, and also as large clumps or clones, derived from a single seed. The species is native from northern Mexico north to the southwestern United States, particularly in southern Texas but also New Mexico. The plants grow in dry soil, often under shrubs. The buttonlike tubercles of the plant are chewed fresh or dry as a legal narcotic drug by certain Native American peoples. There is concern that the American native plants, mostly in southern Texas, are in danger of decimation from ranching, since most of the plants are on private land, and not subject to conservation legislation. Coupled with this is the fact that although harvesting by a few licensed dealers is permitted, this does not ensure a future supply, and commercial cultivation in the United States is not permitted (although numerous companies advertising on the internet offer plants). The future preservation of Mexican plants is similarly in a state of uncertainty.

Peyote has been used by Native Americans since pre-Columbian times. It was regarded as a medicinal panacea. The Spanish Conquistadors instituted the first anti-

drug laws in the western part of the world by outlawing the peyote religion and the use of its sacred peyote. However, the Indians observed their religion in an underground fashion. The Native American Church is a Native American religious group which combines fundamentalist Christian doctrine and Native American moral principles. The movement began among the Kiowa in Oklahoma about 1890. The sacramental food of the group was peyote, and the members came to be known as peyotists. In 1918, peyotists from several tribes incorporated their movement as the Native American Church. The church is said to have over 250,000 members (claims of 400,000 are often made) in the United States, Mexico, and Canada, and is considered to be the most widespread indigenous contemporary Native American religion. The Native American Church has maintained peyote-eating as an essential ritual. The peyote rite lasts from sunset to sunrise, and is usually held in a Plains-type tepee. The rite has four major elements: prayer, singing, eating the sacramental peyote, and contemplation. Peyote is said to produce a mental state in which there is feeling of closeness to ancestors and the Creator. In 1970, the state of Texas legalized peyote for use by Native Americans in religious ceremonies. In 1964, the US court upheld the right of members of the Native American Church to consume peyote during religious ceremonies, and a US federal law confirming this protection was enacted in 1995. For others, peyote is a controlled substance, and possession is illegal in the United States and Canada.

Peyote is a masticatory that is chewed like tobacco, betelnut, khat, and coca leaf. It is ingested principally by indigenous people in Mexico and the United States to produce visions. It is also used occasionally as an illegal, recreational drug, and severe penalties are associated with such unauthorized use. The mushroomlike crown (peyote button, or mezcal button) is cut off and chewed, brewed into a concoction for drinking, or rolled into pellets that are swallowed. Usually from four to a dozen buttons are eaten (some Indians have been observed to ingest up to 50 buttons at one sitting). The most important active substance in peyote is the bitter-tasting, hallucinogenic alkaloid mescaline. Since mescaline is soluble in hot water, it is readily extracted into tea, and this is a common alternative form of consumption. Both the brew and the buttons are extremely bitter, and many novice users have difficulty consuming enough to notice any effects. Moreover, many novice users become so sickened by the taste that they forever abandon the idea of trying peyote as a new (and generally illegal) drug experience. Some users ingest a Dramamine pill half an hour prior to ingesting peyote in order to increase their tolerance. After the initial feeling of nausea, mescaline produces visions and changes in perception, time sense, and mood. The drug is not considered to be physiologically habit-forming.

Medicinal Usage & Potential

Aside from traditional herbal usage by Amerindians, peyote is not used medicinally.

Functional Food Usage & Potential

No usages have developed.

Nutraceutical Usage & Potential

No usages have developed.

Summary Assessment

Peyote is not used nutritionally, and given the very small size of the plant, extremely slow growth, and adaptation to extreme hot, dry conditions, it is most unlikely that the species could become a crop. This is the least promising plant examined in this paper for development as a nutritional source.

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[Place Fig. 13 & 14 in the following section]

Tobacco – *Nicotiana tabacum* L.

Family: Solanaceae (potato family)

Background Information

Tobacco (Fig. 13) is a herbaceous annual (or less commonly a biennial), growing 1–3 m in height. The stem tends to become woody at its base. The flowers are white, yellow, pink, purple or red, 3–6 cm long. Leaves vary in size depending on variety, and the lower ones are often longer than 50 cm. The leaves of cigar-wrapper varieties are thin, fine-textured and small-veined, while those of plug and pipe tobacco varieties are usually coarser, tougher, and thicker. The plant is modified by removing the top, usually when 8 to 12 leaves have developed, as well as branches that are stimulated to grow as a result. This causes the remaining leaves to increase in size by as much as 50%, increases nicotine content, and encourages even ripening of the leaves. The species is thought to be a hybrid, whose ancestors are distributed in the eastern Andes Mountains of South America. Tobacco from *N. tabacum* is produced in most temperate and tropical regions of the world, and is a major crop of many nations.

In addition to *N. tabacum*, *N. rustica* L., known as wild tobacco and Aztec tobacco, was domesticated for tobacco production, although it is not grown commercially in North America. Like the main tobacco species (*N. tabacum*), it is thought to have arisen as a hybrid, probably from ancestral species in Peru, and it does not have a natural native distribution. The name “wild tobacco” is a misnomer, since the species arose in cultivation and has no natural wild distribution area. When Europeans came to North America in the 15th and 16th centuries, both *N. tabacum* and *N. rustica* were widely cultivated by the Indians. *Nicotiana rustica* was the first species to be bought back to the Old Word, but *N. tabacum* was imported soon afterwards and quickly became much more popular. *Nicotiana rustica* is a course South American annual, hardier than *N. tabacum*, and is naturalized in eastern North America, occurring as far north as southern Ontario. *Nicotiana rustica* was widely grown by North America Indians, and was cultivated for tobacco by them as recently as the middle of the 20th century. Tobacco was first cultivated by European colonists in Virginia in 1612, and the species first grown was *N. rustica*. It is now very rarely cultivated in North America, although it is grown in Europe and Asia for smoking tobacco and as a source of the insecticide nicotine. The dried leaves of *N. rustica* contain up to 10% nicotine, whereas those of regular tobacco usually have 1.5-4% (although up to 8% is possible).

Smoking tobacco is not entirely an American (i.e. New World) invention. Australian aborigines also used several Australian species of *Nicotiana* for the purpose, and it appears that people native to the southwestern Pacific may have also used local species of the genus. Perhaps ten species of *Nicotiana* containing the alkaloid nicotine were used by native peoples for religious and medicinal purposes.

The distribution ranges of these species were extended by such usage before European colonization. The earliest record of the use of tobacco is a 5th century Mayan temple in Mexico, where a bas-relief (sculpture with very little depth on a wall) shows a priest smoking.

Tobacco has extremely serious health hazards, and has killed more humans in history than any other plant substance. A recent analysis suggested that about 500 million people alive today will eventually be killed by tobacco use. Smoking tobacco is a cause of emphysema and lung cancer, heart disease, and numerous other disorders. It has been said that smoking is the largest cause of preventable death. It has been estimated that each cigarette smoked takes 5 minutes off one's life, a figure that indicates that smoking a pack of 20 cigarettes a day shortens an expected year of life by 1 month. Smoking is one of the most common causes of "accidental" fires. It is also a cause of social unrest, with the addictive qualities of tobacco causing otherwise thoughtful people to subject innocent passers-by to the deleterious effects of the disgusting habit.

Tobacco is used as a fumitory (i.e. for smoking) in pipes, cigars, and cigarettes, inhaled as a powder (snuff is simply finely ground tobacco), chewed as plugs, and savored by covering the gums with a fine powder. "Smokeless" tobacco includes snuff that is inhaled, and all material that is taken orally—so called "spit tobacco." Chewing tobacco is in several forms. Finely shredded tobacco is dipping tobacco (really not much different from snuff), pressed bricks and cakes are called plugs, and rope-like strands are called twists.

Tobacco has a long history (note Fig. 14). It was chewed by New World Indians. In the United States chewing tobacco was so prevalent in the late 1800s that over 90% of tobacco factories only made chewing tobacco, and spittoons were far more common than ash trays. Chewing tobacco was so popular during the latter 19th and early 20th centuries that 12,000 brands were registered in the United States. Today, the practice of chewing tobacco has remained most popular in the United States, where it has been associated with cowboys and sports, notably baseball, where the stimulant value of nicotine may have been the motivation. At the end of the 20th century, smokeless tobacco was used by about 15 million Americans, and in the United States about 6% of men aged 18 and older (chewing tobacco is primarily a male practice) were using some form of spit tobacco.

Chewing tobacco is addictive, and is not, contrary to the belief of many, safer than smoking tobacco, although the set of health hazards are somewhat different than for smoking tobacco. The nicotine in chewing tobacco has similar adverse affects as

that in cigarettes. Tobacco placed in the mouth is associated particularly with cancers and other pathological conditions of the mouth, tongue, lips and throat. Studies have found that half to three quarters of spit tobacco users have oral lesions. Chewing tobacco users are four times more likely than non-users to develop tooth decay.

In early times in South America, some Indians classified tobacco as a food—occasionally using it as an additive (for example to *chicha*, the maize beer consumed by Peruvian Indians). In modern times, tobacco is occasionally used as a spice. A culinary tobacco fad recently developed in some of the most exclusive restaurants of the world. For example, in the fashionable Michel Rostang restaurant in Paris, the dessert menu has featured "Havana cigar with Cognac mousse," a cigar-shaped creation actually made with crumbled Cuban cigars. In the United States, tobacco-laced cocktails have included the "nicotini" (tobacco-flavored martini) and the "Black Lung" (tobacco-flavored Kahlua). In the United States, the Food and Drug Administration does not permit tobacco as a food ingredient because it not safe, so that it can not be used by commercial manufacturers to produce and sell edible products. Restaurant food, however, is not regulated by the agency. The use of pipe and cigar tobacco by some chefs to impart spiciness to food is limited and likely to remain so, given the toxicity and negative image of tobacco. Nicotine gum is a prescription product which, like the nicotine patch, is intended to assist tobacco users to overcome their addiction gradually.

Nicotine, first chemically isolated in 1807, is extremely toxic. One or two drops (60–120 mg) of pure nicotine placed on the skin can kill an adult human. A typical cigar contains enough nicotine to kill two people, if injected into their bodies. Species of *Nicotiana* have been used as dart-poison ingredients in South America.

Medicinal Usage & Potential

From the 1500s to the 1700s, tobacco was sometimes prescribed by doctors to treat ailments such as headaches, toothaches, arthritis, and bad breath. The idea that tobacco smoke can be beneficial persisted down to modern times. Today, the chief medicinal usage of tobacco is simply to furnish nicotine for the purpose of curing people from nicotine addiction.

Functional Food Usage & Potential

The World Health Organization's Farm and Agriculture Organization in 1981 raised the possibility of extracting protein from tobacco plants as a means of alleviating world hunger. The project has not subsequently received significant

funding, in considerable part because tobacco has become a pariah crop in the eyes of many people. The project has been the subject of research at North Carolina State University. The possibility remains of producing nicotine-free "tobacco-burgers," either as simulated meat, or actual meat of animals raised and fed on tobacco. As discussed below, recombinant proteins are being produced using genetically modified tobacco, and therefore there is an excellent possibility that health-promoting tobacco-based protein additives could become very important as functional food components.

Nutraceutical Usage & Potential

Tobacco has been used as a source of rutin. The chemical rutin is considered to be a compound with "vitamin P" (supposedly anti-viral) activity. Rutin is also an antioxidant, i.e. a substance that counteracts the free radicals produced by metabolism in the body and thought to be damaging. Rutin can be obtained from members off the Rutaceae family, notably lemons and oranges.

It is as a "factory" for molecular farming that tobacco has the greatest significance for both nutraceuticals and pharmaceuticals. Tobacco has been described as an ideal platform for producing recombinant proteins for the following reasons (Daniell et al. 2001, Rymerson et al. 2002, Twayman et al. 2003):

1. Tobacco already has a well-established technology for gene transfer and expression, and is easily genetically manipulated.
2. Tobacco already has a large-scale processing infrastructure.
3. Tobacco already has a long history as a successful crop system for molecular farming.
4. High biomass yield: potentially 100 tonne ha^{-1} (tobacco can withstand several crop cuttings annually).
5. High soluble protein levels.
6. As a non-food/feed crop, containment is less of an acute problem (i.e., little risk of contaminating food or feed chains).
7. Most production systems are based on accumulation of proteins in leaves, eliminating the need for flowering
8. Prolific seed production (up to a million per plant).
9. There is a need to explore alternative uses of this hazardous crop
10. Although many tobacco cultivars produce high levels of toxic alkaloids, low-alkaloid varieties can be used to produce pharmaceutical proteins; also, alkaloid-

free tobacco cell suspensions can be used.

Summary Assessment

Despite being widely despised, tobacco has excellent potential for the production of pharmaceuticals, nutraceuticals, and components for functional foods. Although tobacco is a very useful plant to use for molecular farming, it still has some drawbacks, including the necessity of removing alkaloids, and the persisting negative image of the plant.

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Discussion and Conclusions

The world's most widely used illegal narcotic plant, *Cannabis sativa*, is being actively and successfully developed as a source of new pharmaceuticals, nutraceuticals, and functional food components. For the most part, its success in these respects exceeds that of the other popularly used narcotic plants. Analysis of the reasons for its success provides a basis for predicting the probability of similarly successfully developing of other socially-condemned, dangerous plants, with particular reference to pharmaceuticals, nutraceuticals, and functional foods. The success of *Cannabis sativa* is due to the following considerations.

1. Varieties are available that are, for practical purposes, almost completely lacking in the narcotic constituents.

2. Although it is the source of an illegal narcotic, *C. sativa* is also the source of a wide variety of popular useful products, including pharmaceuticals, nutraceuticals, and functional food components. The demand for the non-narcotic products has been sufficiently high to generate substantial political support for authorized cultivation.

3. A very important consideration has been the need for new diversification crops in *temperate* climates, to which *C. sativa* is suited. The richest countries are in temperate climates, where financial support and research expertise tend to be more available than in many tropical locations.

4. *Cannabis sativa* has a long history of being cultivated as a field crop, so that its agronomy is very well understood. It is easily grown, and very productive.

5. A very large proportion of the world (more so than for any other narcotic, with the exception of tobacco) has personally experimented recreationally with the drug. On the scale of perceived seriousness of narcotics, marijuana is viewed by many as relatively benign.

In the following table, a crude comparison of the eight narcotic species discussed in detail in this paper is give with respect to the above five considerations.

Table 1. Comparison of five considerations determining likelihood of development of eight narcotic species as sources of pharmaceuticals, nutraceuticals, and functional food components.

Narcotic species	Available non-narcotic varieties	Source of popular alternative products	Good candidate to diversify temperate agriculture	Developed as a field crop	Perceived harmfulness
Marijuana	yes	yes	yes	yes	moderate
Opium poppy	no[1]	yes	yes	yes	high
Tobacco	no	yes	yes	yes	high
Coca	no	no	no	yes	high
Betel nut	no	no	no	yes	moderate
Khat	no	no	no	yes	moderate
Kava	no	no	no	no	moderate
Peyote	no	no	no	no	high

[1] until recently

Like the hemp plant, opium poppy is primarily useful as a medicine because of the presence of well known narcotic chemicals, and it is probable that new pharmaceuticals will be based on these. Both plants produce edible seeds and seed oil, with very promising nutraceutical, cosmeceutical, and functional food product possibilities. Licensed cultivation is permitted in many countries, and so there are excellent prospects for the development of new nutritionally significant products.

The tobacco plant seemed destined until recently to continued reduction in importance. With its development as a molecular farm crop, however, it appears to have a promising new life as a source of pharmaceuticals and nutritionally important compounds.

The remaining five narcotic crops (coca, betel, khat, kava, and peyote) are adapted to hot climates, away from the temperate regions where the heaviest investment is presently occurring in plant biotechnology and product research. Given their negative images and substantial lack of past usefulness except as narcotics, these species are unlikely to attract much interest for development for legitimate products. This is unfortunate because research might discover ways of converting the narcotic species to the production of innocuous, needed products, and so provide employment for the substantial numbers of people currently dedicated to the plants.

To date, the predominant approach to eliminating the narcotics problems of the world has been eradication of the plants in question. Indeed, serious efforts have been made to genetically engineer pathogens for the purpose of eradicating narcotic species—a very dangerous approach that could have unforeseen and uncontrollable consequences for non-target crops. Experience with the marijuana and opium plants has demonstrated that it is not difficult to grow legitimate versions of these crops, despite the existence of illegitimate plantations. While controlling narcotics is complex, research should be conducted to examine the possible benefits of converting narcotic species into respectable crops. This may not only benefit local economies, but also reduce the narcotics trade, as land that is dedicated to the narcotic species could be converted to growing non-narcotic varieties of the same species.

Captions for figures

Fig.1. Marijuana (*Cannabis sativa*). Female plant at left, male plant at right.

Fig.2. Hemp oil in capsule form sold as a dietary supplement.

Fig.3. Cosmeceutical products offered by the Body Shop. (“Chanvre” is French for hemp.)

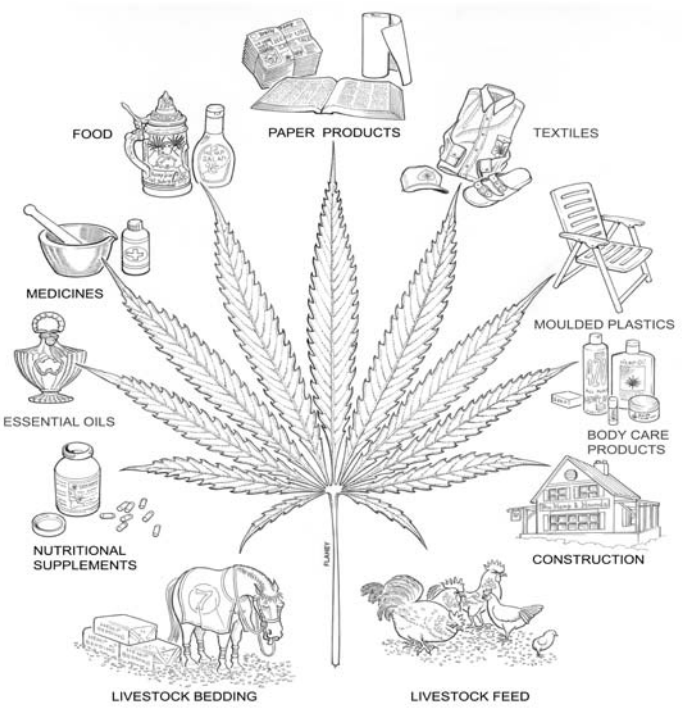

Fig. 4. Major uses of *Cannabis sativa*.

Fig. 5. Opium poppy (*Papaver somnifrum*).

Fig. 6. Coca plant (*Erythroxylum coca*), the source of cocaine.

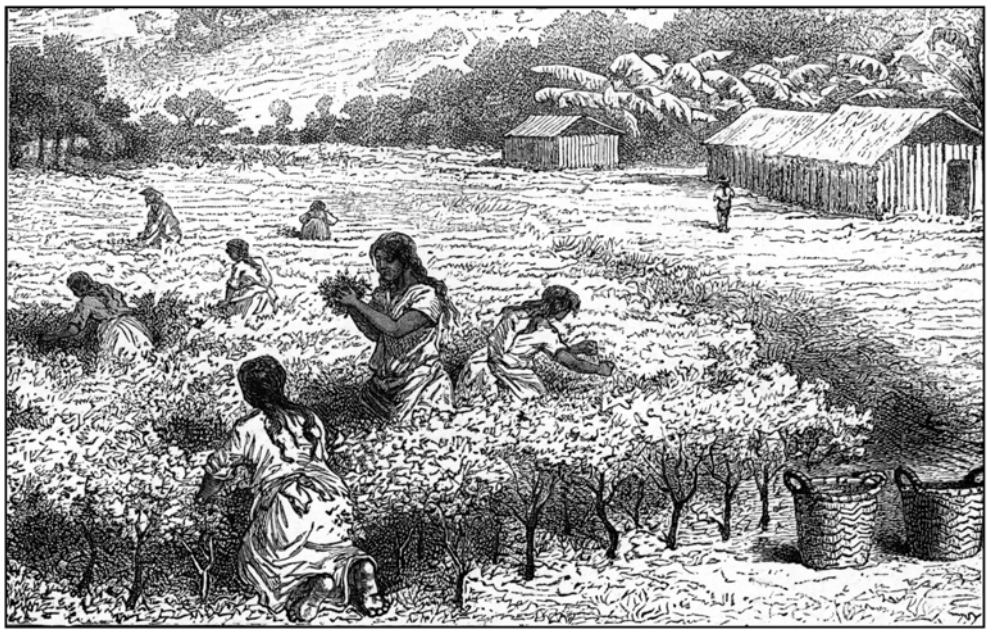

Fig. 7. A nineteenth century coca plantation.

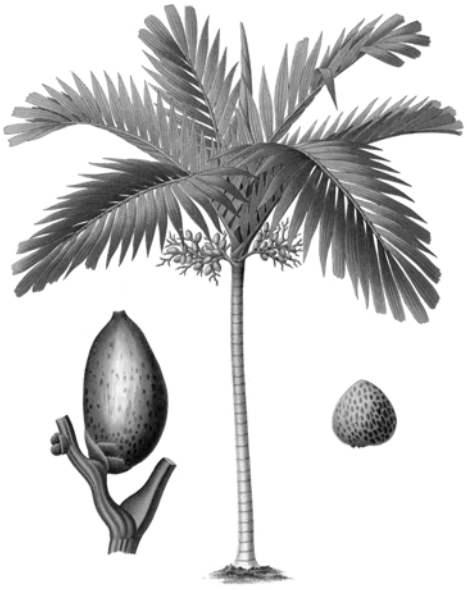

Fig. 8. Betel nut (*Areca catechu*).

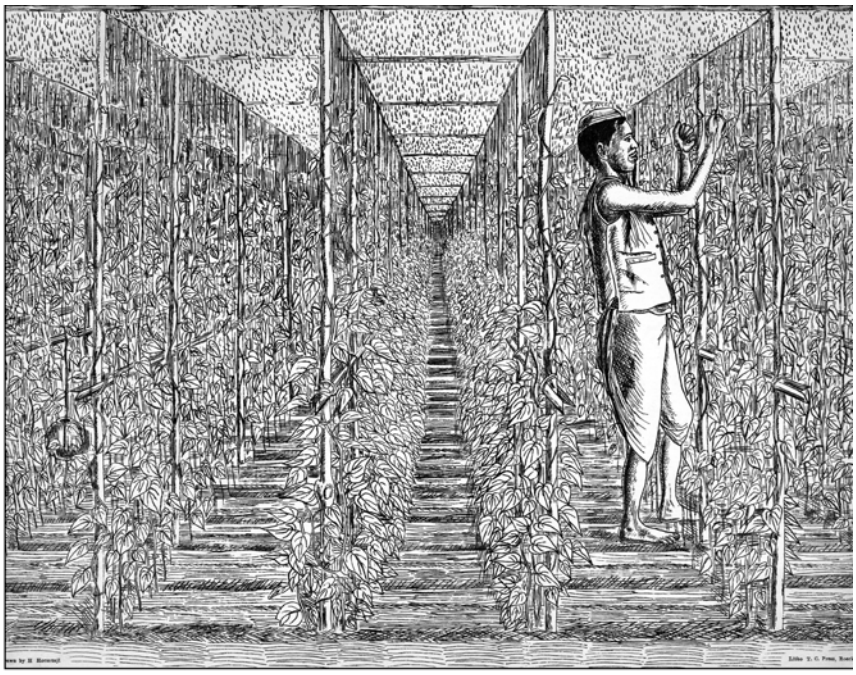

Fig. 9. Betel pepper (*Piper betle*) shade house in India.

Fig. 10. Khat (*Catha edulis*).

Fig. 11. Kava (*Piper methysticum*).

Fig. 12. Peyote (*Lophophora williamsii*).

Fig. 13. Tobacco (*Nicotiana tabacum*).

Fig. 14. Smoking through the ages.