CHAPTER 1

Plants and Human Health

On a recent trip to China, I visited one of my PhD colleagues from graduate school, a Canadian with Chinese roots who saw a business opportunity to start a biotech company in his country of birth. Ever the entrepreneur, he told me of his plans to examine and evaluate a Chinese plant that he thought showed great potential as a new drug. The plant in question has thrived in the fields of his ancestral home as far back as any of his family can remember, and it has been used for generations as a general folk remedy and disinfectant. My colleague felt positive that we were looking at a plant that could have enormous value as a novel form of antibiotic, and perhaps could even offer a solution to the problem of multiple drug-resistant bacteria experienced by hospitals all over the world. I was a little reluctant at first about the concept of using natural compounds as medicines; it seemed in some way to be counterintuitive to my scientific background in biotechnology. My colleague, known among his friends to be a shrewd and rather good plant biochemist, seemed nonplused about my apparent misgivings. A search through available scientific publication and herbal medicine databases yielded no evidence that singled out this particular plant as possessing any known medicinal properties that had been recorded previously. As far as we could tell, we were entering uncharted territory. I gradually gave in to my curiosity and decided to follow my colleague on this "bioprospecting" expedition.

The first step was to see whether the results that my colleague anticipated could be reproduced in a laboratory setting. The initial experiment was simple enough to perform. We ground the plant up into a powder, dissolved this powder in a variety of different chemical solvents, and tested these extracts on different strains of bacteria. We found to our delight (and my amazement) that some of the extracts stopped bacterial growth completely! The next rational step seemed straightforward enough in principle: could we identify what active compound(s) in the plant is(are) responsible for inhibiting the bacteria? From a practical standpoint, this is not necessarily as easy as one would imagine. Biological molecules can be intrinsically complex, and although we could think of some logical directions in which to proceed, it seemed unlikely that we were going to come up with a tangible result for quite some time.

With great enthusiasm, nonetheless, we began to discuss the implications of our results more thoroughly. Had we discovered a new medicine? If so, would it be wise to ensure that our discovery was protected by a patent? Had we tapped into a gold mine? That point brought up more concerns. Did we have a right even to be thinking in terms of value and intellectual property? We may have been the first to test this plant using a standard scientific approach, yet the plant in question had been known by the locals of the region to have medicinal properties for as long as anyone could remember. Surely these people should have some right to this discovery.

Thinking along the lines of intellectual property, it was entirely possible that we had merely identified an already known natural compound, only from a different plant source. Had we actually "rediscovered" a chemical compound that wasn't novel at all, but perhaps was present in other plant species and had already been developed and marketed as a drug or a herbal medicine? The answer wasn't clear.

The more we dwelled on our discovery, the more sober our thoughts became. What if the plant component, which worked so well on a Petri dish (under in vitro conditions), worked much less convincingly on an actual person who suffers from bacterial infection (under in vivo conditions). It's true that there are many unofficial claims of the plant's ability to cure people of infection, but no actual documented proof of this existed. The only available evidence was from the affirmation of the local community. What if the plant had adverse effects on people or interacted with other medicines that one might be taking concurrently? How much would one need to take in a single dose and how would it be administered? Would it be provided as a tea or as a pill, for example? There must be some regulatory format that we should follow to ensure that our plant compound is unique, works in the way that we predict, and is safe to use. It seemed to me that surely all of these questions needed to be addressed before it was time for my colleague and me to celebrate.

Our thoughts turned to existing herbal medicinal products that are available on the market today. What about these sorts of products? Have the active components been identified? Do they actually work and are they safe? Do we really know that much about them at all? Furthermore, are any of the plants or other natural products used derived from endangered species? Does the process of collecting specimens impact the biodiversity of the region? Are there laws in place to protect against environmental damage from people collecting these plants? My colleague assured me that the plant we used in our initial experiment was common enough in the area, and the sample we had used for our experiments was from his family's garden. Our circumstances seemed harmless enough, but surely that is not always the case for the sampling of other natural bioactive compounds.

Other, more philosophical questions came to mind as we continued to discuss the project. What is the relationship between the traditional use of medicinal plants and modern medicine today? What role will plants have with respect to human health in the future? It was an attempt to answer these sorts of questions that led to the premise for this book. The search for the answers was definitely a journey to strange and unusual places. Beginning with our Paleolithic ancestors, this book moves on to cover our complex and fascinating involvement with plants, as both foods and as sources for medicines. The pathway leading from natural plant products to modern drug discovery is discussed. The delicate balance between maintaining biodiversity, the rights of indigenous tribes, and the identification and exploitation of novel bioactive compounds is examined. This book touches on the general spirituality associated with plants used as medicine, ranging from ancient Confucian and Ayruvedic philosophies to actual connections with witchcraft and on to widespread beliefs continued today in African cultures and others. The ways that traditional and conventional medicines merge and complement one another are discussed. The book continues with a glimpse into the changing yet equally important role of plants as novel innovative medicines and as "functional foods" that provide preventive measures against chronic diseases. This book underscores the importance of devising new ways to think about plants and agriculture in general, not only to address a soon-to-be burgeoning world population but also to help us to navigate our way through the impact of climate change. The book concludes with a projection of the role of plants in human health for next 100 years and presents possible means by which plants can play a predominant role in shaping our future.

OUR EARLY RELATIONSHIP WITH PLANTS

How were plants involved in our development into the beings we are today, in terms of the shape of our digestive tracts, our select dietary niches, and even the evolution of our social communities? It has become perfectly clear that a plant-based diet can play a role in helping us to avoid many of today's chronic health problems such as diabetes, high blood pressure, stroke, and some cancers. Did early hominids encounter the same chronic diseases? Do our diets today in some way fail to meet our true nutritional needs? Can crops be designed and bred to improve our health?

The overwhelming majority of primates consume plants as the substantial part of their diet; animal matter constitutes only a small proportion of their food source. Early primates, including man, most likely ate a wide number and diversity of plants that resided in their tropical rainforest homes; these happen to be dicotyledonous plants and would include the ancestors of many fruits, roots, and leafy vegetables that we consume today. Over time, early hominids left the forest and entered savannah regions, where the principal plant species to be found are monocotyledonous, such as cereals and grains. Were our digestive tracts adaptable enough to make the switch to these less traditional plant foods?

In addition to plants, many primate species supplement their diet with some animal matter, including insects and small mammals or birds. The digestive tract of some primates largely reflects these omnivorous food choices; humans, for example, tend toward a larger volume of small intestine and smaller colon than do gorillas, strict consumers of leafy plants, who exhibit the inverse ratio of gut proportions.

Clues with regard to the dietary niches of early humans are scant in evidence and high in conjecture. The reconstruction of prehistory can be ambiguous; and it is difficult to make any broad conclusions. Data have been collected from a variety of sources, including the dietary patterns of closely related primates, early hominid tooth micro-wear patterns, analysis of bone growth, density, and other skeletal pathologies. Together, much of this does not provide an adequate representation of what actually took place; rather, these data symbolize a small sample size of what has been archaeologically preserved.

Upon entry into the savannah setting, early man likely had to cover large ranges of land in search of food. The focus of diet changed to large game, which was complemented by vegetable-like foods. In their continuous search for food, early hominids became bipedal in terms of locomotion. What motivated the switch from largely a plant-based diet to one composed of animal meat and fat? The hunter-gatherers of temperate to Arctic regions of the world seem to have followed this transitional pathway, perhaps in the need for more calorie-rich foods, or perhaps the increased fat intake derived from eating game helped them to survive and flourish in colder climates. As humans became more proficient hunters of other animals, they changed their behavioral patterns as they developed new strategies by which to capture their prey.

The Paleolithic Age then led to the Neolithic Age, when the hunter-gatherer became an agriculturalist. It is still unclear what led to the transition.

Some experts attest that a rapid increase in population led to a strain on the customary food supply; others have suggested that changes in climate may have altered the availability of animals to hunt as meat. In the Middle East, these changes in climatic conditions led to the favored growth of grassy plants such as wild wheat, rye, and barley. Faced with a dwindling supply of animals to hunt, early man naturally turned to grain cultivation. Doing so meant a significant change with respect to lifestyle. Gathering wild grain when it ripens and loses its seed to the wind requires large groups of people to be available at the right place and at the right time to catch the harvest. This in turn would require the development of settlements to be at the ready for the time of harvest. Using a scenario such as this, the hunter-gather may have morphed into the first farmer.

At first, this may have involved at most the smallest of efforts, for example, by cutting back the vegetation so that a patch of a particular species of plant that was good to eat could receive more sunlight and the space to thrive and grow. Other primitive methods involved the selective burning of old growth vegetation to encourage the rapid growth of tender edible leaves and shoots, either for human consumption or to sustain grazing for large game animals in proximity to the hunter-gatherers. Plant tubers and roots that were found to be tastiest and most nutritious were most likely collected; a few were transplanted and left to propagate in designated areas to ensure a future food source. Such forms of land management by early "proto-farmers" were practiced in one form or another more than 10,000 years ago by many of our Neolithic ancestors throughout the Americas, the Middle East, and Asia.

It was only a matter of time before what can only be called the first true plant breeder began to emerge, as early man learned crop cultivation as a means of ensuring reliable future harvests. One possible scenario that led to this revolution in our history is the collection and preservation of select seeds at the end of each growing season. The act of selecting seeds to be spread at the beginning of each new season most likely took place at a subconscious level at first, in response to the quality of each season's crop. Early farmers learned that scattering some of the seeds they had collected from their best harvests ensured them of more of the same for the next year's growing season. Perhaps the particular seeds that the first farmers chose to be saved for future sowing produced food crops that had larger yields, were tastier, or ripened more readily. This selection of seeds from the most suitable crops was man's first attempt at deliberately breeding for the traits he desired, and thus altering the course of gene flow for a given population. It is safe to say that the predictability of this arrangement soon led to the establishment of a co-dependence of man and plant. The end result was the domestication of crop plants and the emergence of

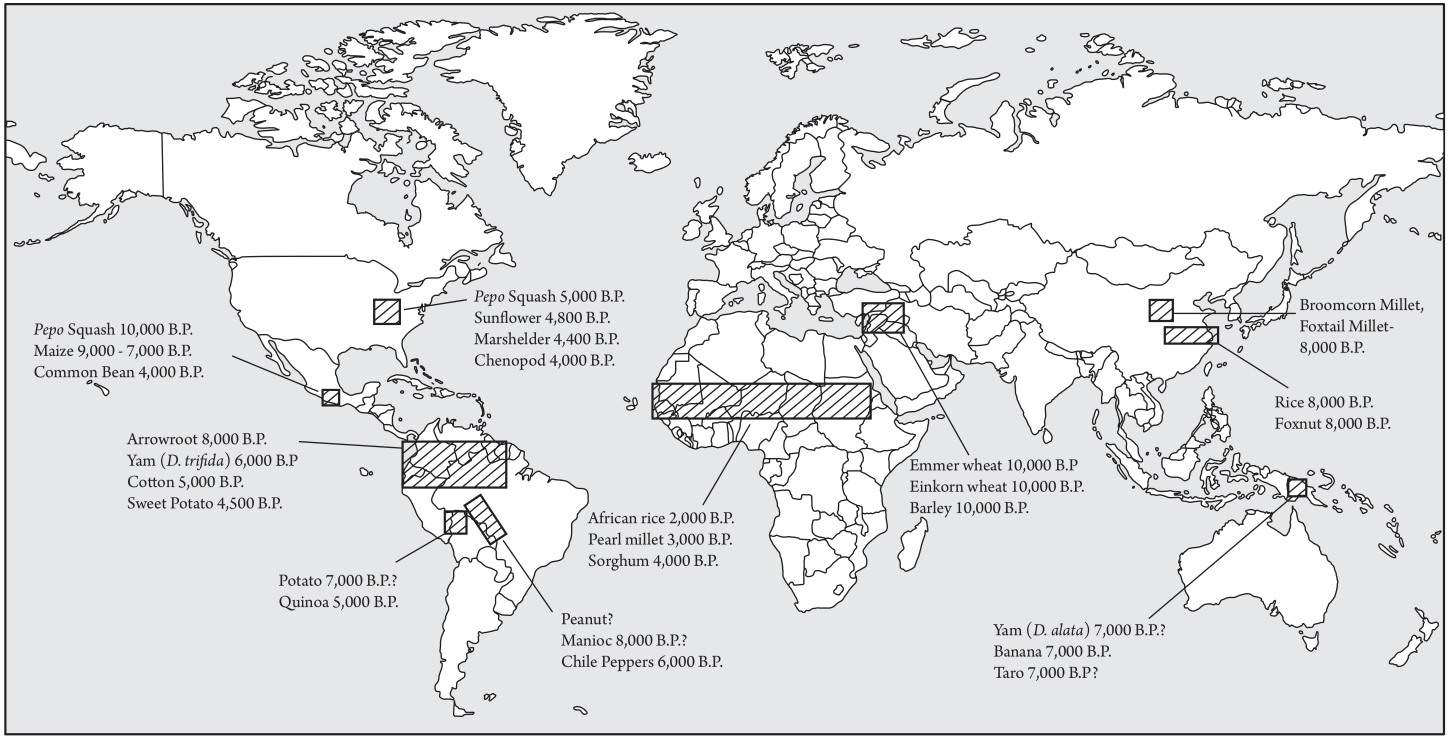

Figure 1.1.
Currently recognized independent centers of plant domestication. From *Proceedings of the National Academy of Sciences, U.S.A.* 103, no. 33 (August 15, 2006): 12223–28.

early inhabitants into what we recognize today as civilized society, one in which a variety of occupations in addition to agriculture were required so that the settlement as a whole could function smoothly.

Many of the crops the world uses today as staples were first domesticated by approximately 6000 BC (Figure 1.1). Man's active participation in breeding for select traits was not sufficient to make early crops such as barley or wheat a staple in the diet, however. It was clear that raw grain itself was indigestible; some processing mechanism had to be set in place to thresh and grind the grain, store it for future use, or cook it so that it was suitable for eating. Irrigation systems were devised to ensure a consistent water supply and thus reliable harvest in times of drought. Trading routes were established between different settlements, so that a variety of foods, and later other material goods, could flow to distant lands. It is around this time that distinct cultures began to materialize (Figure 1.2).

While large fields of grain were becoming the first domestic staple crops in the Middle East, early farmers in many other parts of the world were plotting small gardens containing a wide assortment of fruit trees, vegetables, herbs, spices, and a variety of medicinal plants. In some of these primitive societies, crop plants were attributed a supernatural reverence, perhaps even viewed in some instances as "gifts of the gods," as is the case of corn in Mayan cultures. Plants that were used for medicinal purposes were often associated with an aura of mysticism, and treatment of the sick involved distinct healing rituals performed by an appointed individual who was believed to be a link to the spirit world. The relationship between plants and health as it relates to dietary habits and therapeutic choices of healing remains richly steeped in custom, taboo, tradition, and spirituality even to this day.

An eclectic mix of herbalism with spirituality is showcased in the health practices of many cultures that exist in the present, such as traditional African medicine. Distinct from the reductionist, analytical approach of Western medicine, traditional African medicine takes into account the role that ancestral spirits have on an individual and the surrounding environment as direct links to people's health and well-being. With the number of Western medical doctors too small to address the current population, traditional healers and remedies made from indigenous plants remain critical to the health of millions of Africans to this day (Figure 1.3). Furthermore, modern pharmaceuticals are often hard to come by or are too costly. Indeed, over 80% of the world's people rely on herbal remedies rather than modern drugs, and traditional herbal practitioners are their only means of medical expertise.

The evolutionary path from Paleolithic to modern man sounds straightforward enough, but nutritionally speaking, nothing is that simple. While

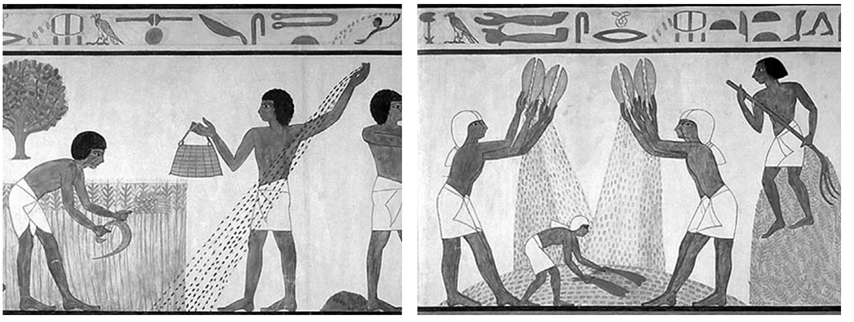

Figure 1.2.
Agricultural workers in ancient Egypt.

Figure 1.3.
A traditional healer in Uganda treating a patient's dizziness. From Africa Renewal, United Nations.

one would assume that cultivating crops, consuming more plant and less animal matter, settling into towns and cities, and establishing sophisticated trading routes must directly indicate improved health of man in general, a proportion of data suggests otherwise. A comparison of skeletal pathologies of hunter-gatherers and farmers suggests that farmers were in general more prone to infection, had a shorter life expectancy, and experienced more chronic malnutrition than their hunter-gatherer counterparts. It seems, according to this argument, that substituting a meat-based diet for one that is grain-based had a detrimental impact on our overall health.

Often these data have been used to support the popular "Paleo Diet," a high meat, low carbohydrate diet that is embraced by many today as what our true eating lifestyle should be. The reasoning is that since we have the same genetic composition as our hunter-gatherer ancestors, our style of life and dietary choices should mimic theirs. Our current diet contains plant-based foods high in carbs, such as breads, potatoes, rice, and pasta; these were introduced only recently as food sources and thus are associated with a number of modern diseases we face today, such as diabetes, heart disease, and some cancers, many of which can be directly linked to diet. Did these diet-related diseases increase with the evolution of agriculture?

While a high-carb diet and sedentary lifestyle have been blamed for many ills of modern society, several points contradict the assumption of better health for our earlier ancestors. First, although the sequence of our genes matches those of our ancestors, our epigenetic profile, or the way these genes are expressed, may differ substantially. In addition, our civilization has brought with it a life expectancy of over 70 years, an age unheard of in prehistoric times. Overconsumption of meat and fat makes post-reproductive individuals more prone to succumb to heart disease at later stages of life; however, the life span of Paleolithic man was not long enough to experience these conditions. As Reay Tannahill puts it in *Food in History*,

> On the principle that twentieth-century diseases are largely a product of the twentieth-century diet, they recommend a return to the foods of our ancestors (dates unspecified), who did not die—as so many people do today—of cardiac thrombosis, strokes, or cancer.
>
> This is perfectly true. Our ancestors died, instead, of malnutrition, diabetes, yaws, rickets, parasites, leprosy, plague, skin infections, gynecological disorders, tuberculosis, and bladder stones, and they usually died in their 30s. Most modern diseases do not develop until the victim is in their 40s or 50s. If our ancestors lived 10 years longer, coronary thrombosis, strokes and cancer might have been their fate too.[1]

So the dogma for a diet high in meat is not without fault. Alternatively, one can equally argue that a hazard of strict vegetarianism is the difficulty in securing sufficient nutrients for optimal health. Arguments regarding the benefits and pitfalls of animal- versus plant-based diets are engaging, and the taboos associated with food throughout various cultures are fascinating in their own right. This book, however, is about plants and their current role in human health, and it is with this brief history of man's beginnings that this book commences.

Plants, unlike most animals, are immobilized to one place; they cannot flee or fight off their predators. Instead, they have devised different means to avoid being eaten; they can be thorny, bitter to taste, and poisonous.

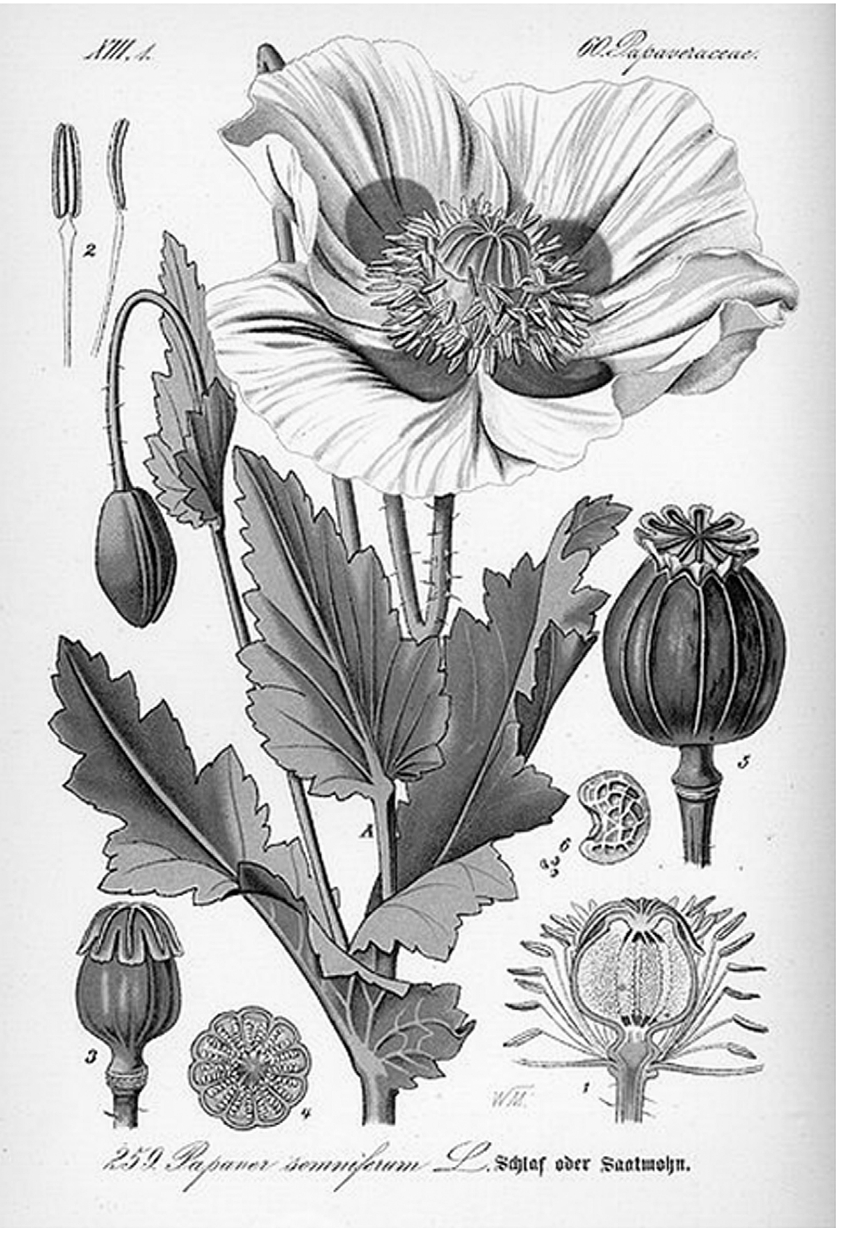

Figure 1.4.
(a) Opium poppy (*Papaver somniferum*).

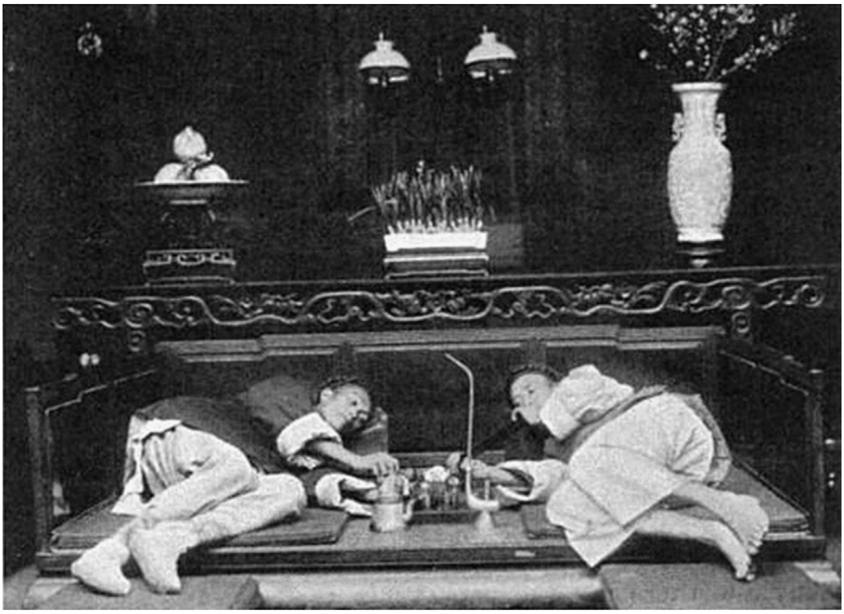

Figure 1.4.
(**b**) A Chinese opium house, photograph circa 1900.

They can contain anti-nutrients, compounds such as phytates that prevent valuable minerals from being absorbed in the digestive tract, making them less attractive as a food source. Any and all of these features help to deter them from being eaten, and foragers are warded away from consuming specific plant species that exhibit these attributes. Oddly enough, it's among plant chemicals, or phytochemicals, that so many of our medicines are found. Among the plant-derived drugs used as medicinal compounds throughout history and even today are morphine and digitalis. For example, the pain reliever morphine is produced from the opium poppy, as are heroin and codeine (Figure 1.4).

Many plants possess bioactive compounds that can help ward off chronic illnesses, such as cardiovascular disease and even some cancers. Lycopene, a compound found in tomatoes, and anthocyanin, found in blueberries, are examples of anti-oxidants—plant compounds that are abundant in a wide assortment of fruit and vegetables. The use of plants as functional foods to prevent chronic diseases is outlined in detail in Chapter 5. Different plant compounds can even be expressed in different anatomical parts of the plant, such as the roots, leaves, and flowers. Alkaloids, for example, can be extremely poisonous to humans but a number, like morphine, atropine, and cocaine, are widely used in medicine. As the next chapter will reveal, bioactive compounds derived from plants and other forms of nature lie at the root of modern drug discovery.