1.1 Common Roots of Pharmacotherapy

From a historical perspective, the production of medicines and the pharmacologic treatment of diseases began with the use of herbs. Methods of folk healing practiced by the peoples of the Mediterranean region and the Orient found expression in the first European herbal, De Materia Medica, written by the Greek physician Pedanios Dioscorides in the first century AD. During the Renaissance, this classical text was revised to bring it more in line with humanistic doctrines. The plants named by Dioscorides were identified and illustrated with woodcuts, and some locally grown medicinal herbs were added. Herbals were still based on classical humoral pathology, which taught that health and disease were determined by the four bodily humors—blood, phlegm, black bile, and yellow bile. The humors, in turn, were associated with the elemental principles of antiquity: air, water, earth, and fire. The elements could be mixed in varying ratios and proportions to produce the qualities of cold, moist, dry, or warm—properties that also were associated with various proportions of the four bodily humors. Thus, if a particular disease was classified as moist, warm, or dry, it was treated by administering an herb having the opposite property (Jüttner, 1983). Plant medicines were categorized by stating their property and grading their potency on a four-point scale as "imperceptible," "perceptible," "powerful," or "very powerful." Opium, for example, was classified as grade 4/cold. A line of association that linked sedation with "cooling" allowed the empirically known sedative and narcotic actions of opium to be fitted into the humoral system. Pepper was classified as grade 4/dry and warming. The goal of all treatment, according to Hippocrates, was to balance the humors by removing that which is excessive and augmenting that which is deficient" (H. Haas, 1956). Humoral pathology obviously developed into one of the basic principles of conventional medicine.

The monographs that appeared in herbals typically consisted of an illustration of the healing plant, the name of the plant and its synonyms, its action (potency grade and property), and the indications for its use. Indications were not stated in the modern sense of disease entities but as symptoms. For example, cough, catarrh, and hoarseness were each considered separate illnesses. The monograph concluded with a detailed account of the various preparations that could be made from the herb. By and large, the authors of herbals were not laypersons but doctors trained in conventional medical schools. The herbals were written not just for doctors but also for the "com-
mon man,” in some cases for the express purpose of serving as a guide “when the doctor is too expensive or too far away” (quoted in Jüttner, 1983).

Prior to 1800, when medicine entered the scientific age, traditional herbal medicine was the unquestioned foundation for all standard textbooks on pharmacology. It was not until the advent of “medical science” that phytotherapy was relegated to the status of an alternative modality. From the historical perspective, however, it is incorrect to classify phytotherapy as a special or alternative branch of medicine. When we consider that the history of classical herbal medicine spans more than 2000 years from antiquity to modern times, it is reasonable to assume that many of the medicinal herbs used during that period not only have specific actions but are also free of hazardous side effects. Otherwise they would not have been passed down so faithfully through so many epochs and cultures. It would be frivolous to dismiss the collective experience of more than 50 generations of patients and physicians as a “placebo effect” (Benedum, 1998).

1.2 Making Medicines Safer by Isolating and Modifying Plant Constituents

In his famous “Account of the Foxglove” published in 1785, William Withering described how he was called to the home of an itinerant salesman in Yorkshire. “I found him vomiting incessantly, his vision was blurred, and his pulse rate was about 40 beats per minute. On questioning, I learned that his wife had boiled a handful of foxglove leaves in a half pint of water and had given him the brew, which he swallowed in one draught to seek relief from asthmatic complaints. This good woman was well acquainted with the medicine of her region but not with the dose, for her husband barely escaped with his life.”

Cardiac glycosides of the digitalis type have a very narrow range of therapeutic dosages. Exceeding the full medicinal dose by just 40% can produce toxic effects. The dosage problem is compounded by the large qualitative and quantitative variations that occur in the crude plant material. Depending on its origin, the crude drug may contain a predominance of gitoxin, which is not very active when taken orally, or it may carry a high concentration of the very active compound digitoxin.

Thus, isolating the active constituents from herbs with a narrow therapeutic range (Fig. 1.1) and administering the pure compounds is not simply an end in itself. This scientific method of medicinal plant research is, rather, the means by which very potent constituents can be processed into safe medicinal products. The goal is not to concentrate the key active component but to obtain a pharmaceutical product that has a consistent, uniform composition. Processing the isolated constituent into pills, tablets, or capsules results in a product that is diluted by pharmaceutical excipients. For example, the concentration of digitoxin in a digitoxin tablet is approximately 10 times lower than in the original digitalis leaf.

With the development of the natural sciences and the scientific method in medicine beginning in the early 19th century, herbal remedies became an object of scientific analysis. The isolation of morphine from opium