



FIGURE 1.1 Chemical structures of four naturally occurring classical therapeutic agents.

with the biological target, the compound further has to fulfill a multifaceted set of criteria before it can be safely administered to patients. Absorption, distribution, metabolism, excretion (ADME), and toxicology studies in animals and humans are time-consuming research tasks which often call for redesign of the chemical structure of the potential therapeutic agent investigated. It is an iterative process which in reality ends up in an overall compromise with respect to multiple desired properties.

1.2 DRUG DISCOVERY: A HISTORICAL PERSPECTIVE

In early times, there was no possibility of understanding the biological origin of a disease. Of necessity, progress in combating disease was disjointed and empirical. The use of opium, ephedra, marijuana, alcohol, salicylic acid, digitalis, coca, quinine, and a host of other drugs still in use long predate the rise of modern medicine. These natural products are surely not biosynthesized by plants for our therapeutic convenience, but they normally have survival value to the plants in dealing with their own ecological challenges.

The presence of biologically active substances in nature, notably in certain plants, was in medieval times interpreted more teleologically. In the early sixteenth century, the Swiss-Austrian medical doctor and natural scientist Paracelsus formulated the “Doctrine of Signatures”:

Just as women can be recognized and appraised on the basis of their shape; drugs can easily be identified by appearance. God has created all diseases, and he also has created an agent or a drug for every disease. They can be found everywhere in nature, because nature is the universal pharmacy. God is the highest ranking pharmacist.

The formulation of this doctrine was in perfect agreement with the dominating philosophies at that time, and it had a major impact on the use of natural medicines. Even today, remanences of this doctrine can be observed in countries where herbal medical preparations are still widely used. Although the “Doctrine of Signatures” evidently is out of the conception of modern medicinal natural product research, the ideas of Paracelsus were the first approach to rational drug discovery.