erally considered to be the narcotic morphine, marketed by Merck in 1826 [118]. The first semisynthetic pure drug based on a natural product, aspirin, was introduced by Bayer in 1899.

3 NATURAL PRODUCT RESEARCH AND DEVELOPMENT—AN UPDATE

The World Health Organization estimates that approximately 80 percent of the world's population relies primarily on traditional medicines as sources for their primary health care [44]. Over 100 chemical substances that are considered to be important drugs that are either currently in use or have been widely used in one or more countries in the world have been derived from a little under 100 different plants. Approximately 75 percent of these substances were discovered as a direct result of chemical studies focused on the isolation of active substances from plants used in traditional medicine [29, 30]. The number of medicinal herbs used in China in 1979 has been estimated to be numbered at 5267 [115, 116]. More current statistics based on prescription data from 1993 in the United States show that over 50 percent of the most prescribed drugs had a natural product either as the drug or as the starting point in the synthesis or design of the actual end chemical substance [118]. Thirty-nine percent of the 520 new drugs approved during the period 1983 through 1994 were either natural products or derivatives of natural products [65]. Indeed, if one looks at new drugs from an indication perspective over the same period of time, over 60 percent of antibacterials and antineoplastics were again either natural products themselves or based on structures of natural products. Of the 20 top-selling drugs on the market in the year 2000 that are not proteins, 7 of these were either derived from natural products or developed from leads generated from natural products. This select group of drugs generates over 20 billion U.S. dollars of revenue on an annual basis [60, 65].

Drug development over the years has relied only on a small number of molecular prototypes to produce new medicines [65]. Indeed, only approximately 250 discrete chemical structure prototypes have been used up to 1995, but most of these chemical platforms have been derived from natural sources.

While recombinant proteins and peptides are gaining market share, low-molecular-weight compounds still remain the predominant pharmacologic choice for therapeutic intervention [60]. Just a small sampling of the many available examples of the commercialization of modern drugs from natural products along with their year of introduction, indication, and company are: Orlistat, 1999, obesity, Roche; Miglitol, 1996, antidiabetic (Type II), Bayer; Topotecan, 1996, antineoplastic, SmithKline Beecham; Docetaxel, 1995, antineoplastic, Rhône-Poulenc Rorer; Tacrolimus, 1993, immunosuppressant, Fujisawa; Paclitaxel, 1993, antineoplastic, Bristol-Myers Squibb.

The overwhelming concern today in the pharmaceutical industry is to improve the ability to find new drugs and to accelerate the speed with which