I. INTRODUCTION

Plants have formed the basis for traditional medicinal systems for thousands of years, with the first records dating from about 2600 BC in Mesopotamia. Peoples used oils from cedar and cypress, licorice, myrrh, and poppy juice, among other things, substances that are still in use today for the treatment of a variety of illnesses and infections. Ancient Egyptian, Chinese, and Indian documents show that medicine in these societies included numerous plant-based remedies and preventives. The Greeks and Arabs both contributed substantially to the assimilation, codification, and development of plant-based medicines. The isolation of the active principles from the plants and herbs such as strychnine, morphine, and colchicine began in the early 1800s [Newman et al., 2000; Dev, 1999; Fallarino, 1994].

Today approximately 80% of the world’s population relies on traditional plant-based medicines for primary health care. The remaining 20% of the world’s population also depends on plant products for health care [Arvigo & Balick, 1993; Farnsworth et al., 1985]. About 25% of prescription drugs dispensed in the United States contain plant extracts or active ingredients derived from plants. Out of a total of 520 new drugs approved for commercial use between 1983 and 1994, 30 were new natural products and 127 were chemically modified natural products.

Despite the great successes already achieved in natural products chemistry and drug development, we have barely begun to tap the potential of our molecular diversity. Only an estimated 5% to 15% of the 250,000 species of higher terrestrial plants in existence have been chemically and pharmacologically investigated in systematic fashion. The percentage of insects, marine organisms, and microbes investigated is far lower still. In the case of microbes, it is estimated that 95% to 99% of existing species are currently not even known, never mind analyzed. There is currently great interest in exploring extreme habitats for useful enzymes from microbes, including acidophiles (from acidic sulfurous hot springs), alkalophiles (from alkaline lakes), halophiles (from salt lakes), thermophiles (from deep sea vents), and psychrophiles (from extremely cold waters) [http://www.aaas.org/international/africa/sgbd/11b.html, Nnadozi et al., 2000].

Others have been designed based around the natural ligands of known drug targets. For example, albuterol is based on the hormone adrenaline and binds to the same receptor.

Today, more systematic approaches are used. High-throughput screening is used to test thousands of potential targets with thousands of diverse chemical compounds in order to identify promising lead compounds (chemical entities that interact with targets and therefore have potential as drugs). The alternative method of rational drug design involves the design
and synthesis of compounds based on the known structure of either a specific target or one of its natural ligands. The results of the Human Genome Project and Human Pathogen Genome projects provide many new potential drug targets. For this reason, target identification must be followed by target validation, which confirms the likelihood that interfering with the target protein will impact on the disease.

The development of a new therapeutic drug is a complex, lengthy and expensive process. It can take from 10-15 years and over 500 000 000 $ to bring a drug from concept to market. This includes 2-4 years of pre-clinical development, 3-6 years of clinical development and additional time for dealing with the regulatory authorities (fig. 1) [http://www.wellcome.ac.uk/en/genome/tacklingdisease/hg09b005; Abrantes-Metz et al., 2003].

![Phases in drug development](http://www.wellcome.ac.uk/en/genome/tacklingdisease/hg09b005.html)

**Figure 1.** Phases in drug development [http://www.wellcome.ac.uk/en/genome/tacklingdisease/hg09b005.html].