Chapter 60

The Role of Plants in the Drug Discovery Program of the United States National Cancer Institute


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Through the ages, humans have relied on plants as a source of medicines for the treatment of a variety of diseases. Sophisticated traditional medicine systems, mainly based on the use of plants, have been in existence for thousands of years in countries, such as China (Chang & But, 1986) and India (Kapoor, 1990). It has been estimated by the World Health Organization that about 80% of the over 5 billion inhabitants of the world rely mainly on traditional medicines for their primary health care (Farnsworth et al., 1985). Plant products also play an essential role in the health care systems of developed countries. Analysis of data on prescriptions dispensed from community pharmacies in the USA from 1959 to 1980 indicate that about 25% contained plant extracts or active principles derived from higher plants, and at least 119 chemical substances, derived from about 91 plant species, can be considered as important drugs currently in use in one or more countries (Farnsworth et al., 1985).

Plants have a long history of use in the treatment of cancer (Hartwell, 1982), though the majority of claims made for the efficacy of such treatment may be viewed with skepticism, since cancer is likely to be poorly defined in terms of folklore and traditional medicine. The United States National Cancer Institute (NCI), however, recognized the potential value of plants as sources of new anticancer agents shortly after it established its Cancer Chemotherapy National Service Center (CCNSC) in 1955. The aim of CCNSC was to coordinate a national program for the procurement and screening of plant materials for chemotherapeutic activity, and to develop and evaluate any active agents as potential drugs for the treatment of cancer. In 1960, a systematic effort to collect and screen plants was initiated in collaboration with the United States Department of Agriculture (USDA). Between 1960 and 1982, 35,000 plant collections were made by USDA, mainly from temperate regions in over 60 countries, and screened against a range of animal tumor systems, and a large number of agents belonging to a wide variety of chemical classes were isolated (Suffness & Douros, 1979; Hartwell, 1976). Few of these new agents, however, satisfied the stringent preclinical development requirements and advanced to human clinical trials. The present discussion will be limited to the plant-derived agents that have advanced to clinical trials.

60–1 STATUS OF PLANT-DERIVED ANTICANCER AGENTS

The best known of the plant-derived anticancer agents are the so-called Vinca alkaloids, vinblastine and vincristine, isolated from the Madagascar periwinkle (Catharanthus roseus) (L.) G. Don. These drugs first became available in the 1960s, and are now used in the treatment of a wide variety of cancers, including leukemias, lymphomas, and testicular cancers (Neuss & Neuss, 1990). They are still produced from C. roseus cultivated worldwide. Two other agents in regular clinical use are etoposide (VP-16) and teniposide (VM-26), which are prepared semi-synthetically from epipodophyllotoxin, an epimer of podophyllotoxin isolated from Podophyllum peltatum L. or P. emodii Wall (Jardine, 1979). Etoposide is used in the treatment of small cell lung and testicular tumors, and lymphomas and leukemias (O’Dwyer et al., 1985).