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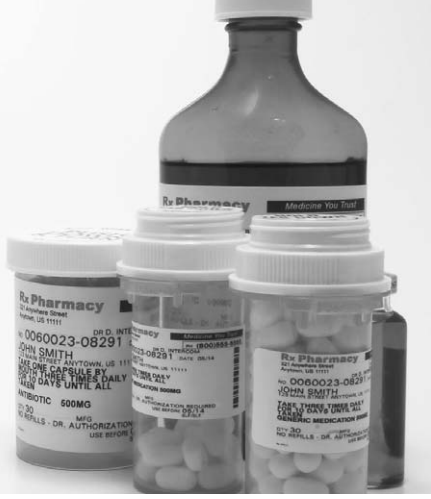
Ethnobotany & The Process of Drug Discovery: A Laboratory Exercise



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It is well known that global biodiversity is being lost at an alarming rate (e.g., Wilson, 1992; Lawton & May, 1995; Pimm et al., 1995). The loss of a species not only impoverishes the community of which the species was once a part, but these losses also affect humans. Biodiversity has economic value to humans and many suggest that of all groups who should be most interested in the preservation of biodiversity, it should be industries leading the way, as biodiversity has provided, and will continue to provide, many raw materials used by industries around the world. This is especially the case for the pharmaceutical industry, as extinction results in the "... loss of raw materials for existing and new weapons in the fight to alleviate human suffering and prevent death" (Grifo et al., 1997). In order for students to fully appreciate the value of biodiversity, especially the value of species as sources of new drugs, it is important to understand the process of drug discovery more completely. This laboratory exercise was designed to help students understand important steps that are part of the actual drug discovery process, while at the same time, help them appreciate the value of biodiversity as a source of new and important drugs to treat a range of human diseases.

Figure 1. Color prints of plants closely related to species that are important sources of two antimalarial drugs; *Cinchona succirubra* Pav. (actually, *C. pubescens* Vahl., one of the species that are a source of quinine) on the left, and *Artemisia absinthium* L., closely related to *A. annua* L. (source of artemisinin) (images from Rare Books from MBG Library, © 1995 - 2005 Missouri Botanical Garden, http://www.illustratedgarden.org).

○ Natural Products & The Process of Drug Discovery

How important is biodiversity as a source of prescription drugs? A number of studies reported that from 25% to 57% of prescription drugs sold in the U.S. or worldwide have at least one active compound that now or was once derived or patterned after compounds isolated from natural products (Grifo et al., 1997; Newman et al., 2003; Butler, 2004). Natural products are especially important as sources of new cancer drugs (Mann, 2002; Newman et al., 2003; Cragg & Newman, 2005) and as antiparasitic agents (Tagboto & Townson, 2001; Newman et al., 2003), including antimalarial drugs. One of the first effective antimalarial drugs was quinine, derived from the bark of the cinchona tree, while one of the newest and most effective antimalarial drugs currently available, artemisinin, was first isolated from the herb, *Artemisia annua* (Hien & White, 1993; Klayman, 1995; Dhingra et al., 2000; Figure 1). Artemisinin has been found to have potential as a cancer drug as well (Singh & Lai, 2001; Lai & Singh, 1995; Lai & Singh, 2006). Although some drug companies have restricted their natural product screening programs, many still believe that the natural world will continue to be our most important source of novel molecules effective in treating a wide array of human diseases.

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One of the biggest hurdles we face when considering natural products as sources of new drugs is the question of which species to screen. For example, there are now estimated to be approximately 421,968 species of flowering plants (Bramwell, 2002), but only about 11% of these species have been screened phytochemically (Verpoorte, 1998). This is unfortunate, as many drugs currently being used are derived from plants, including some of the best-selling drugs on the market (Farnsworth et al., 1985; Baker et al., 1995; Newman et al., 2003). Also, the "hit rate," the rate at which the screening of