Discovery of New Drugs from Plants

Dr. H.R.W. Dharmaratne, Senior Research Fellow, Natural Products, IFS

The use of plants in medicine dates back to the beginning of mankind, and Medicinal chemistry, in its crudest sense has been practised for several thousand years. Man has searched for cures of illness by chewing herbs, berries, roots and bark, because plants being the most abundant and easily accessible, were the first to be tried out in time of sickness. This way primitive man started to experiment with the plants around him in an attempt to treat injuries and cure diseases. Luckily, Some of these early clinical trials were quite successful. Thus over the centuries, by trial and error, he gradually discovered a number of worthwhile remedies.

As civilization began to develop in the Indian sub continent, China, Egypt,South America and the Mediterraneans, the therapeutic potential of a large number of medicinal plants were collected and recorded. In ancient Sri Lanka such information was recorded in Ola leaf scripts. However, not until the last 100-150 years has knowledge of the active constituents of these natural sources been known.

The discovery and the development of the above active compounds into useful medicines may involve,

1. Natural products or synthetic compounds and their biological activity.
2. Synthesis of new compounds
3. Elucidation of their interaction with receptors of various kinds including enzymes and DNA
4. The determination of their absorption, transport and distribution properties.
5. Studies of the metabolic transformation of these chemicals into other chemicals.

Table 1, gives some of the earliest medicines described, their active compounds and historic reference.

Plant	Active Compound(s)	Activity	Reference
1. *Dichroa febrifuga*	Alkoloids	anti malaria	Pentsao (A book of herbs) written by a Chinese Emperor
2. *Ephedra sinica* (Ma Hung)	Ephedrine	heart stimulant, raises blood pressure	Shen Nung about 5,100 years ago
3. *Papaver somniferum* (Poppy)	morphine,codeine	analgesic for coughs, mental disorders	Theophrastus in the 3rd century B.C. Rhazes (Persia) in the 10th century A.D.
4. *Rauwofolia scrpeutina*	reserpine	antihypertensive, for insomnia, insanity	ancient Hindu scripts
5. *Cinchona*	quinine (1820) structures	anti-malarial	A monk named Calancha introduced this to Europe in 1633.
6. *Digitalis purpurea* (foxglove plant)	glycosides digitoxin,digoxin	treatment of congestive heart failure	cited by Welsh physicians in 1250 introduced by Withering in 1785

If the approach to Drugs (chemotherapeutic agents) continued as in ancient times, only few diseases would be treated today in western medicine. Modern therapeutics is considered to have begun with the extraction of foxglove plant which was cited by Welsh physicians in 1250.

Natural products and their derivatives make up a large percentage of drugs in the current market. Typically when a natural product is found to be active it is chemically modified in

order to improve its properties. In general, clinically used chemotherapeutic agents or drugs are not discovered. What is more likely to be discovered is known as a "lead compound". The lead is the prototype compound that has the desired biological or pharmacological activity, but may have many other undesirable characteristics, for example, high toxicity, other biological activities, insolubility or metabolism problems. The structure of the lead compound is then modified by synthesis to amplify the desired activity and to minimize or eliminate the unwanted properties. But two of the rare drugs Penicillin and Librium were discovered without a lead.

References:

1.Richard B. Silverman, *The Organic Chemistry of Drug design and drug action*,1992, Academic Press, Inc.