Paper Presented at Conference on Developments in Forestry and Environment Management in Sri Lanka

Prospecting for Green Gold – Is it a Realistic Goal for Sri Lanka to Pursue or a Mirage?

A.M. Abeysekera

Department of Chemistry, University of Sri Jayewardenepura, Sri Lanka

Throughout history, plants have provided man with the essentials of life – food, clothing, shelter and medicine. Before synthetic organic chemistry developed to its present level of sophistication, almost all the drugs used in medicine were plant derived. Even today about 25% of the drugs used in modern medicine are from plants or based on compounds derived from plants. Some of the most recent highly effective drugs introduced into modern medicine have been from plants, such as the anti cancer drug taxol from *Taxus brevifolia* and the anti malarial drug artimisinine from *Artemisia annua*. Although the pharmaceutical industry had pinned its hopes over the last two decades on combinatorial chemistry to generate lead compounds for drug discovery, these hopes have not been realized, and there is a growing opinion that the emphasis should be shifted to natural products as a source of new drugs^{1,2}. A review of new drugs introduced in the twenty year period commencing in 1981, shows that of the 868 drugs 28% are natural product derivatives and 24% have been created around a natural product based phamacophore³. The untapped potential of plants as a source of new drugs can be realized when one considers the fact that of the estimated 300,000 or so plant species on earth, less than 5% have been adequately investigated by modern scientific methods for their activity.

Sri Lanka has a rich history in the usage of plants for medicine. Apart from the ancient system of Ayurveda, which came to Sri Lanka from India, there is a strong tradition of indigenous medicine (deshiya chikitsa), with both systems relying mainly on plants as the source of drugs. For its size, Sri Lanka is a country with high biodiversity, having over 3000 plant species of which almost one fourth are endemic. It is clear that tropical countries such as Sri Lanka have a resource – the biologically active molecules that lie within its plants – "Green Gold", waiting to be discovered and exploited. Prospecting for this green gold is perceived by many to be a pathway, which through the process of patenting will bring economic benefits to the country.

However, Sri Lanka does not possess the human or material resources to pursue such a goal on its own. The process of drug development starting from the prospecting stage to placing a drug on the market is a complex one and has to proceed through several stages including formulation of the search strategy, obtaining reproducible extracts, screening and discovery of activity, isolation of an active compound, physico- chemical studies, pharmacological studies, pre-clinical testing including structure modifications and formulation, clinical trials and finally regulatory review and registration. The time required for this process could be anything from 12 to 20 years, and the cost could be higher than 500 million dollars. It also requires personnel having expertise in drug development from many different areas of specialization such as chemistry, pharmacy, pharmacology, toxicology, biochemistry and medicine, supported by sophisticated laboratory facilities and support staff. It also requires persons knowledgeable in drug regulatory and patent legislation.

It is clear that if Sri Lanka is to benefit from its "Green Gold" by developing drugs for modern medicine, it can be done only with the collaboration of outside agencies, such as the multinational drug companies or foreign research institutes and universities having adequate resources. Such collaborations brings with it a host of new problems such as the protection of intellectual property with regard to indigenous knowledge, allocation of costs, risks and rewards, returns from royalties and profit sharing . None of these problems are insurmountable. The 1991 agreement between Merck and the Instituto Nacional de

Biodiversidad in Costa Rica is a notable landmark where advance compensation was given for prospected biological material and a share of royalties from new products was ensured⁴. The agreement also included technology transfer, training and technical assistance. There are also now well established protocols for international research collaborations including transfer of biological material. However, given the lack of understanding of the complexity of the process of drug development and the xenophobic attitude of a section of the legislators, and an unenlightened and vociferous "environment" lobby in the media, the chances of any institution in Sri Lanka entering into a collaboration which will bring economic benefits is remote. At present there is some scientific collaboration whose output is restricted to publications in reputed journals.

Given this situation it is important to examine other strategies to exploit our "Green Gold" and the available indigenous knowledge on its usage, for the economic benefit of the country and for the benefit of humanity through providing better drugs for health care. The changing perspectives on traditional medical systems such as Ayurveda brought about by the increased information flow in recent times due to globalization, provides us with an opening for such strategies. Traditional systems of medicine, which were earlier thought to be primitive, ineffective and useful only as a source of leads for the pharmaceutical industry, are today considered to be holistic, cost effective and clinically effective. It is significant that the World Health Organization had incorporated traditional medicine into its programmes in 1976.

Most traditional drugs are polyherbal preparations having multiple active components. These components have different functions with the overall effect on the organism being an interactive function of the individual effects. There is increasing experimental evidence for the operation of synergism in herbal drugs⁵.

There is no scientific basis to believe that the single receptor based "magic bullet" model is the only valid model to use in developing drugs. The fact that most prescriptions carry the names of more than one drug by itself supports the opposite view, namely, that a single active component is often not sufficient to bring about the desired overall change in the patient. The multiple ingredients found in drugs used in traditional medicine could have multiple effects including;

- 1. Reaction with a specific receptor
- 2. Increase the bioavailability of active components
- 3. Generalised effects via the immune/endocrine system
- 4. Reduce side effects

This change of perspective internationally on traditional medicine, coupled with the ever-growing "Back to Nature" movement, which manifests itself in so many ways, provides the opportunity for the exploitation of our "Green Gold". Given the stringent requirements in most countries for the registration of drugs for modern medicine, it is virtually impossible to register complex herbal drugs. However, if good quality standardized products based on traditional knowledge are developed, these could be marketed as health foods, nutraceuticals and non-prescription over the counter drugs. Data on toxicity and efficacy of these products will be essential to fulfill the legal requirements for as well as for successful marketing. To succeed in this effort, scientific inputs and research is needed in the areas of standardization and quality control, and clinical and pharmacological studies of herbal drugs. A major economic advantage of such products is that the raw materials for their production will be available readily only in the countries where the plants are found. These products cannot be "synthesized" easily. Further, if the drugs are traditional drugs they can neither be patented nor stolen.

Two non-material barriers that exist inhibiting developments in this area are, the attitude of Sri Lankan scientists that it is not worthwhile doing research that cannot be published in the so called "indexed

journals" publishing articles on pure science, and the insular attitude of the Sri Lankan medical profession towards alternative/complementary medical systems. It is essential for scientists and doctors to work together to generate the knowledge required to have a thriving herbal products industry.

Conservation of bio-diversity and the economic cultivation of medicinal plants will be important in sustaining a herbal drugs industry. On the other hand, a thriving herbal drugs industry can be made to aid in the conservation of bio-diversity demonstrating the economic value of plants⁶.

To answer the question raised in the title of this article, the development of pharmaceutical for modern medicine based on active compounds isolated from plants, at present is only a mirage; whereas that of developing herbal products based on knowledge of the traditional usage of plants, scientific research and modern technology is a realizable goal.

References

1. Rouhi, A.M. (2003), Rediscovering natural products, Chemistry English News, Vol. 81:41, 77.

2. Lam, K.S. (2007), New aspects of natural products in drug discovery, Trends in Microbiology, Vol.15:6, 279-289.

- 3. Newmann, D.J., Cragg, O.M. and Snader M. (2003), *Natural products as a source of new drugs over the period* 1981-2002, J.Nat.Prod., 66, 1022.
- 4. Zebich-Knos, M. (1997), Preserving biodiversity in Cost Rica: The case of the Merck INBio agreement, J.Env.Dev., Vol. 6:2, 180-188.
- 5. Williamson, E.M. (2001), Synergy and other interactions in Phytomedicines, Phytomedicine, Vol. 8:5, 401-409.
- 6. Abeysekera, A.M.(1988), *Modern alchemy and the economic opportunities of globalization*, Proceedings of Sri Lanka Association of Advancement of Science, Vol. II, 133-149.