

## Development of natural product drugs in a sustainable manner

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### The significance of sustainable development of natural product drugs

For approximately 85% of the world's population, plant materials are a primary source of health care (Fabricant & Farnsworth 2001). This fact is not sufficiently accepted by pharmaceutical companies that are producing synthetic drugs for decades as solutions for incurable diseases. Knowledge of plants and their medicinal properties that were transmitted from generation to generation is in danger of disappearing. Developed countries in alliance with their large pharmaceutical companies, constantly in the struggle for new markets, do not permit the development of local pharmaceutical companies in developing countries.

Although it is generally known that nature provides right solutions in a form of medicinal plants corresponding exactly to the homeland of a particular human community, it often happens that we treat diseases with preparations originating from very distant countries. Even nowadays, we are facing a paradox with the same problem present for centuries: Outside parties frequently manipulate and interfere with local policy makers in order to gain access to local communities' environmental resources. In addition, mainstream science and more developed society exploit environmental knowledge for locating and extracting natural resources, and making use of medicinal plants for commercial purposes. Developing communities or countries

rarely benefit economically. At a time when we are facing global economic crisis, which most severely affects developing countries, assistance in raising their own capacities, including development of renewable natural products, would strengthen the economy of these countries, and economically unburden the rest of the world.

Humankind is not sufficiently aware that natural products drug discovery is important for new generations as a tool for their health care (Cordell & Colvard 2012). We know that for the major lethal diseases, there are no truly effective drug treatments. In addition, drug resistance to existing chemotherapeutic regimens for fungal and bacterial infections, AIDS, cancer, and malaria is increasing. Because of the challenges for health care in the future, this is the call for decision-makers, governments, international agencies, and pharmaceutical companies to commit to the sustainable development of natural products as medicinal agents, particularly in developing countries.

Medicinal plants, both endemic and widespread, their resources and knowledge about their usage must be preserved since these plants could be renewable source for new drugs. It is known that chemicals and chemical reagents are typically non-renewable, and their use depletes our future resources. Consequently, all drug discovery programs, synthetic or natural, must be the concept of sustainability (Cordell 2011).

\* The views expressed in this brief are the author's and not those of the United Nations. Online publication or dissemination does not imply endorsement by the United Nations.

## Perspectives

Plant extracts and products contribute in four major areas to human health and wellbeing:

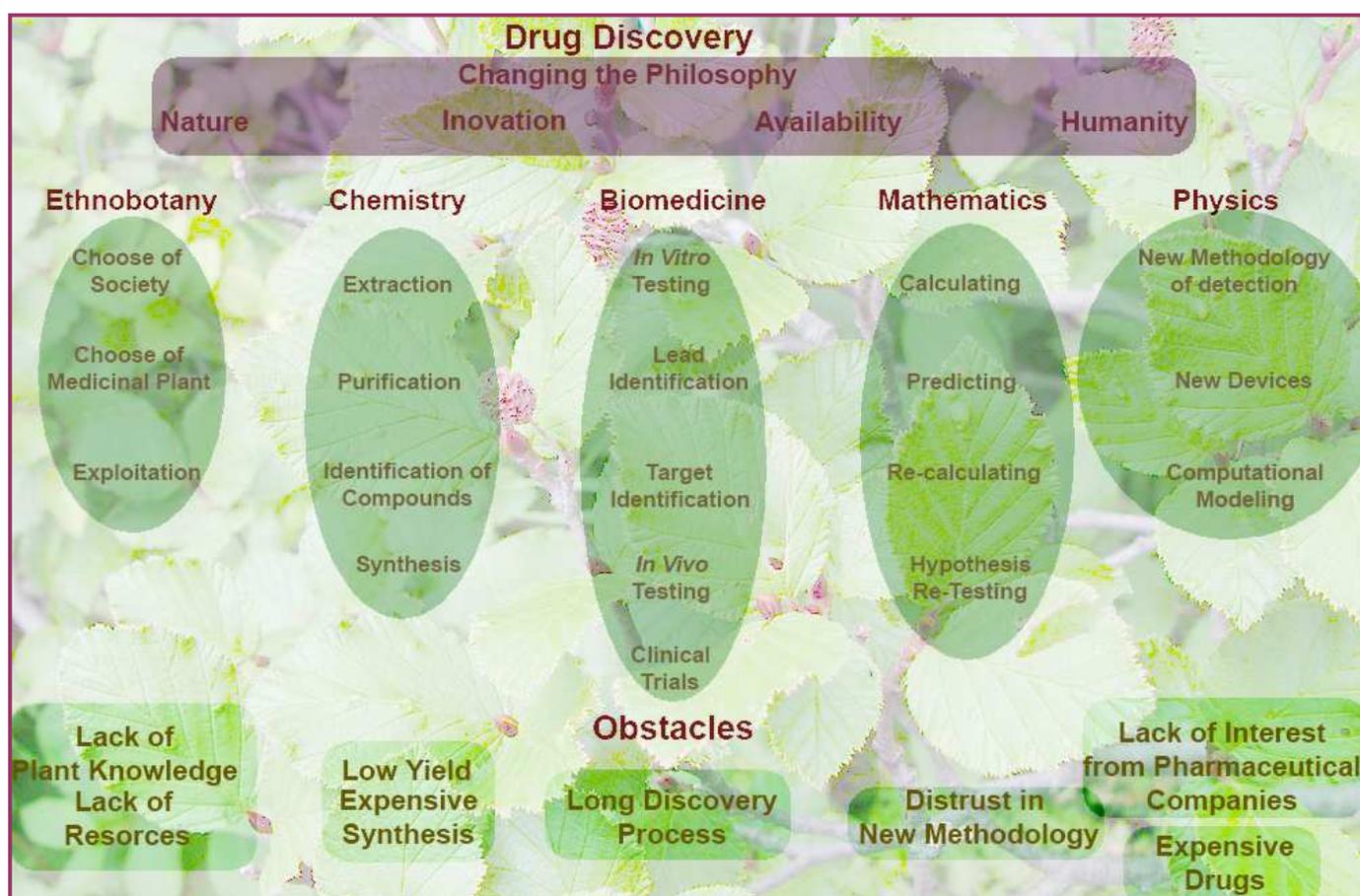
- 1) Foodstuffs,
- 2) Flavoring agents and spices,
- 3) Perfumes and cosmetics, and
- 4) Pharmaceutical and biological agents (Cordell 2004).

Their exploitation in sustainable manner would provide significant commercial perspective to:

- 1) Global pharmaceutical companies,

- 2) Small to medium size biotechnology companies,
- 3) Botanical supplement companies, and
- 4) Food industry (Cordell 2004).

Besides these obvious benefits, development of natural products in a sustainable manner may interface different scientific fields (Figure 1). To achieve this goal, there is a strong need for changing the philosophy and establishing new connections among nature, invention, availability and humanity (Figure 1).



**Figure 1.** Drug discovery from natural sources – a chance for the reunion of natural and human sciences to improve the health care systems all over the world. Changes in the perception of natural treasures and necessity to help developing countries to build their own facilities and engage own scientific potential will ensure sustainable development of natural product drugs. Interdisciplinary research will enable the overcoming of obstacles that are present for many decades in the process of natural products drug discovery.

Biotechnology companies may play crucial role in the sustainable development of natural product drugs. Translocation of the genes from slow-growing to fast-growing, large biomass plants or other organisms will enable the large-scale production of medicinal agents. Although the use of transgenic plants is a questionable for the preservation of biodiversity, genetic engineering will play an important role in saving medicinal plants, which are rare or endangered (Cordell 2011).

The imbalance between humans and other species on our planet is a threat to the survival of the humankind. Therefore, plant ecology should be considered in the sustainable development of natural products. According to the World Wildlife Fund (data from 2004), due to the human consumption, 20% of medicinal plants in the world are in threat of disappearing (Pan SY et al. 2013).

The ethical rules should be considered during the exploitation of medicinal plants. Humankind should not satisfy its own needs at the expense of other Earth species. In less developed countries, plants are the primary source of health care. When large pharmaceutical companies confiscate medicinal plants in order to make new drugs, these drugs will not be available to the local people because of the costs. This is also an ethical issue. Traditionally used plants are far less expensive than the new drugs isolated from them and eventually synthesized (Pan SY et al. 2013).

## **Problems and possible solutions**

Over the past decades, pharmaceutical companies have shown an increased interest in exploring new compounds from plants. However, the lack of a rational approach in many aspects has limited their success.

Pharmaceutical companies often give up from capital investment in the development of natural products because collection of plants in some countries may be a time-consuming process and require extensive (re-)negotiations related to access. Their approach includes bringing as much chemical diversity as possible to the biological screening interface but with no consideration given to the origin of the plant-derived materials. They do not care about chemo-diversity, functional diversity of the constituents, or ethno-medical association of the plant. Another reason for quitting is concern about plant extracts, which frequently yield a known, rather than a novel, active constituent (Cordell 2004).

Certainly, safety issues must be considered before accessing the plants:

- 1) Plant authentication,
- 2) Cytotoxic, mutagenic and therapeutic perspective,
- 3) Free of potentially toxic insecticides, pesticides and heavy metals,
- 4) Free of fungal and insect infestation, and
- 5) Free of radiation contamination (Cordell 2004).

Either as mentioned before, developed countries are not willing to invest, in the people or the places in developing countries because of bureaucracy, cost, and time. Consequently, bio-rich developing countries will not be able to access their biome and enhance their scientific (taxonomic, chemical, and biological) capacity. Local pharmaceutical development will be inhibited. Therefore, developing countries will continue to rely on externally acquired (imported) pharmaceutical and medicinal agents.

Ethno-medical information, biological evaluation of plant extracts and their constituents, the chemistry of natural sources, and the clinical evaluation of plant extracts are still not accessible globally. The useful databases

that are available are Indian plant anticancer compounds database (InPACdb), The herb information Knowledge base (THINKherb), Traditional Chinese medicines integrated database (TCMID) and Traditional Chinese medicine information database (TCHM-ID) (Pan SY et al. 2013).

There is a strong need for indexing eco- and ethno-information of plants, chemistry and biology of their products in such way that information can be analyzed and accessed globally in real time (Cordell & Colvard 2005).

There is another problem regarding access of active principles. They are often extracted and analyzed only at a single moment in time, ignoring daily metabolic flux, seasonal variation in enzyme activities, and the biosynthetic genes which are present, but not fully functional. Development of methodology able to characterize the majority of constituents in an extract without isolation may help in the process of extracts validation and standardization (Cordell 2004).

While there are important ecological concerns regarding genetically modified crops, they present economically effective way to bring preventative health care to humankind (Cordell 2011). There are numerous fungi, bacteria, and, in some cases, algae, symbiotically associated with the plant, which are capable of independent biosynthetic production. Investigation of this potential will enhance the production of active agents in a sustainable manner (Cordell 2004).

We require programs to assist developing countries to potentate their facilities, and scientists in order to evaluate natural product-based medicinal agents in a sustainable manner. This would significantly improve their health care systems.

International efforts and investment in new medicinal agents will require the creation of numerous new alliances. These alliances must work on both local and global level and involve individuals who can set aside their ego for the greater good. Therefore, the alliances should be composed of international agencies, government agencies, pharmaceutical companies, academic institutions, non-government organizations, scientific societies, and private foundations (Cordell 2004).

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This brief is based on the work of Professor Emeritus Geoffrey A. Cordell, University of Illinois at Chicago, College of Pharmacy.

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