

## Bioprospecting or Biopiracy? The Pharmaceutical Industry's Use of Indigenous Medicinal Plants as a Source of Potential Drug Candidates

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### Abstract

The field of drug design and discovery is at a crossroads. The supply of potential new small molecule drug candidates has lagged behind the development of novel protein drug targets. As a result, the pharmaceutical industry has increased its efforts in obtaining plant species thought to exhibit biological activity from developing countries. This 'bioprospecting' has led to claims of 'biopiracy,' whereby drug companies that are patenting and selling pharmaceutical agents derived from indigenous plant species do not provide financial compensation for the traditional knowledge or royalties earned from the sales of the drugs to the source countries of the plants. Potential solutions exist that could remedy the problems; however, there is still a great deal of work to be done to ensure the system functions in a way to protect the interests of the developing countries. Establishing equitable and binding agreements between the parties may be the only way to ensure a long-term, sustainable, mutually beneficial relationship.

### Introduction

A new world of drug design has opened up with the sequencing of the human genome. Scientists are using this knowledge to better understand the functions and interactions of proteins, leading to more effective strategies in designing molecules to block or enhance the actions of proteins involved in many disease processes. This collaboration of genetics, biochemistry and organic chemistry has given rise to many new potent pharmaceuticals targeting many diseases; however, there is one major drawback in this vision of future health care. The large number of potential drug targets elucidated has already outgrown the supply of potential drug candidates.<sup>1</sup>

Combinatorial chemistry is a relatively new technology that has allowed chemists to greatly increase production of new synthetic compounds, but it has its limits. Even combining the efforts of



Foxglove, the plant source of the heart medication digitalis.

classical and combinatorial organic chemistry with another new technique called rational drug design – computerized modelling predictions of potentially active molecules – has not been able to keep up with the demand for new molecules to test against the newfound drug targets. “If you asked me what I lay awake at night worrying about today: It’s not genomics. It’s not genetics. I lay awake worrying about chemistry,” commented Peter N. Goodfellow, Senior Vice-President of Discovery at SmithKline Beecham.<sup>1</sup>

With this shortfall of chemical compounds to analyze, the pharmaceutical industry has begun to look again at plants as a principal source of potentially bioactive molecules. This change in attitude is ironic since plants were, before the era of synthetic organic chemistry, once the most popular place to harvest potential drugs in Western medicine. Furthermore, 80% of the world, mostly the ‘undeveloped’ regions, still rely on the indigenous medicinal knowledge of local plants for their medical needs.<sup>2</sup>

### Plants as a Source of Pharmaceuticals

It is well known that plants are an abundant source of medicinal drugs. Between 25-50% of current prescription pharmaceuticals come from plants, either directly or through modifications of biochemical templates harvested from the plants, and the value of drugs to the U.S. pharmaceutical industry coming from plant species is estimated at over 30 billion USD per year.<sup>3</sup> Aspirin, digitalis, cortisone, taxol, ephedrine, curare and novacaine were all initially plant-derived, to name but a few.<sup>3,4,5</sup>

A natural ecosystem like a rainforest acts like its own chemical laboratory, with each species experimenting over time with various chemical defenses to ensure survival in the world of natural selection. They have been synthesizing these compounds for millions of years to protect against predators, infection, pests, and disease. This makes plant species an excellent reservoir of bioactive compounds with the potential for application to treat human diseases. However, it has been estimated that fewer than 5% of tropical plant species have been examined for their medicinal value. This

huge untapped potential, plus the increasing need for new molecules to test, has generated increased interest in the pharmaceutical industry for novel plant-derived compounds. In 1983, there were no U.S. pharmaceutical firms involved in research of plants found in developing countries. Today, there are over 200 corporations and U.S. government agencies studying rainforest plants for their medicinal capacities.<sup>3</sup>

### Bioprospecting or Biopiracy?

With this increase in what is known as 'bioprospecting,' however, another political, economical and human rights issue has arisen: the notion of 'biopiracy.' Bioprospecting is the "exploration, extraction and screening of biological diversity and indigenous knowledge for commercially valuable genetic and biochemical resources."<sup>5</sup> This practice is not new, however. For decades, plant collectors from industrialized countries have ventured southward in search of valuable genetic material for agricultural plant breeding, but no money changed hands in the process, nor was recognition given to the indigenous farming communities who selected, maintained and improved traditional crop varieties.<sup>5</sup> This type of practice has become known as biopiracy, which refers to "the theft of intellectual property, such as genetic resources or traditional plant medicines, from poor communities by multinational companies."<sup>6</sup>

A similar type of prospecting is now occurring in the pharmaceutical industry. Many drug companies are obtaining vast numbers of plants and chemical compounds derived from plants from developing countries and screening them for potential use as pharmaceutical agents. Although this will probably lead to many new disease-fighting drugs, and thus substantial profits for the pharmaceutical industry, there are currently no regulations in place to ensure that the source countries of these plants will be adequately compensated.

How are the pharmaceutical companies obtaining the plant species from the developing countries? According to one report, biotechnology companies are sending scouts around the world – often posing as tourists – to discover plants that potentially have commercial value for the drug industry. Under the guise of ecotourism, local people are employed as 'nature interpreters' to guide visitors in biodiversity-rich places, and to share with them their indigenous knowledge about biological resources and how to use them. These scouts then collect the identified plants and bring them back to their companies for testing.<sup>7</sup>

It has also been reported that locals in developing countries smuggle species of plants out of the country and sell them to pharmaceutical companies for analysis. In Sri Lanka, for example, a botanist was intercepted by customs at the airport trying to smuggle out plant extracts in his suitcase. In the same month, customs officials discovered a container-load of Kothalahimbutu – an herbal medicine believed to control diabetes – being shipped to Japan through a firm owned by a wealthy Sri Lankan.<sup>8</sup>

Once the plants have been analysed, the pharmaceutical companies can patent any potentially active compounds as their own discovery, thereby preventing the source country from having any legal claims to royalties from the sale of the drug. In essence, they escape paying any financial compensation to the country where the biological material or indigenous knowledge first originated. One could argue that these countries should simply patent the drugs

themselves; however, they generally do not have the requisite scientific equipment to analyse the chemical components of their indigenous plants, nor the capacity to pay the international patent fee of 60,000 USD per patent.<sup>8</sup> Therefore, they are unable to compete with the wealthy pharmaceutical companies trying to patent their indigenous medicines.

Recently, however, there have been two court rulings in favour of the rights of the indigenous countries. Product patents are normally given only if they fulfil the criteria of being new, specify the process of production, and have commercial value. If there are discrepancies in this process, the patent can be contested in court, as in the case of the U.S. patent for turmeric, which was successfully challenged by India on the grounds that its medicinal properties have been well-known since ancient times.<sup>8</sup> Similarly, an American firm acquired the patent for a fungicide derived from the seeds of the Neem tree, which flourishes all over Asia, Africa, Central and South America, and is used for many purposes, including as an insect repellent for crops. This patent was revoked by the European Patent Office in May 2000 on the grounds that it was not a new technology.<sup>6</sup> Although these rulings seem encouraging, many countries do not have the wherewithal to fight the multinational pharmaceutical companies in long court battles, and so without change to the current system, the developing countries will probably lose out in the end.

If unpaid royalty payments were being made to developing countries and indigenous peoples for the plant varieties and local knowledge used by multinational food and drug companies, those providers would be earning an estimated 5.4 billion USD a year, says a report commissioned by the United Nations Development Programme (UNDP).<sup>2</sup> Examples of countries not receiving their full share of these royalties include Tibet, India, Sri Lanka, South Africa, Samoa, Madagascar, Ecuador, Mexico and the Philippines.

### Finding Solutions to the Problem

Owing to the lack of adequate compensation for the countries supplying the medicinal plant species, the question of what can be done to bring about change to the current system needs to be addressed. First, we need to assess exactly what the developing countries desire in terms of compensation. Besides an agreement for royalties on sales of pharmaceutical products derived from the plants, an immediate reciprocal exchange would also be very important, since research conducted in any given location may never lead to a commercial product. Without the commitment of immediate compensation by the pharmaceutical companies, it is possible that the developing nations could derive no benefits from their knowledge and assistance if no products ever make it to market. Besides direct financial contribution, it would also be beneficial to provide immediate compensation in the form of supplies and services to the local peoples and to ensure that at least a part of any funding goes to support environmental protection in the regions supplying the plants in order to ensure long-term stability of the natural ecosystems.<sup>9</sup>

A study prepared for the UNDP discussed potential strategies to assist indigenous peoples in claiming biodiversity as their own property and to claim financial royalties owed to them by industry. The proposed steps in this new "intellectual integrity framework" are as follows:<sup>2</sup>

1. Consultation with indigenous communities to learn what steps they wish to take to preserve biodiversity and to properly acknowledge their contributions.
2. New deposit rules that would identify biological 'inventions' as to their origin, including names of individuals or communities in developing countries, when they are deposited in gene banks or when patent application is made. Failure to provide such 'passport data' could nullify a patent.
3. A rule that would make any material in gene banks and cell libraries collected from indigenous communities off-limits for patent claims by others.
4. Appointment of ombudspersons in industrial-country patent offices to investigate complaints from indigenous communities and their national governments. This person would have authority to delay patent approvals and require review of patent applications.
5. Tribunals that could resolve disputes between indigenous communities and patent claimants.
6. The creation of a fee structure in each patent jurisdiction that would pay for expenses incurred by indigenous communities for deposits, tribunals and legal representation.

#### Some Companies are Trying to Help

Although some pharmaceutical companies are exploiting developing countries for their resources without compensation, there are others who have made strides to reciprocate financial rewards to these nations in the form of investments and promised royalties. Shaman Pharmaceuticals is a U.S. company that discovers and develops novel pharmaceutical agents from tropical plants with a history of medicinal use. At its induction in 1990, Shaman instituted internal guidelines for reciprocity to indigenous cultures and countries that contributed knowledge and resources to its medicinal plant discovery efforts. Shaman outlines short-, medium-, and long-term support measures in its guidelines, which serve to provide financial, infrastructure, technology, and sustainability support to the peoples and countries from which it derives its pharmaceutical products.<sup>10</sup>

Although Shaman's efforts are to be commended, it has been reported that some local peoples are less than satisfied with the overall experiences with Shaman. In Tanzania, locals expressed disappointment that Shaman did not live up to its reciprocity standards. The report goes on to state that if Shaman had spent more time trying to understand and adhere to the local healers' perceptions and priorities, the company could have easily made the healers more satisfied with respect to their own wishes and needs.<sup>10</sup>

Another pharmaceutical company that has made efforts to reciprocate compensation is Merck and Company. In 1991, Merck invested over 1 million USD to Costa Rica's Instituto Nacional de Biodiversidad (INBio) bioprospecting project. INBio agreed to collect and provide samples from so-called 'wild' plants, insects and microorganisms to drug-screening scientists at Merck laboratories for medicinal assay. If the compounds prove useful and any resulting drugs make it to market, Merck will give INBio an undisclosed share of the royalties, of which 50% will be set aside for conservation projects through Costa Rica's National Park Fund.<sup>3,10</sup>

Thus far, however, the Merck-INBio agreement has not produced any major revenue-producing drugs.<sup>1</sup> Regardless, Merck has provided continuing support for the project; a published report states that, as of 1999, Merck had invested more than 3.5 million USD to the project.<sup>11</sup> Despite Merck's efforts, this level of financial compensation is relatively insignificant compared with what the pharmaceutical industry, as a whole, realistically owes to the indigenous countries for the knowledge and biological resources they have supplied for many years.

#### Conclusions

Despite the allegations of 'biopiracy,' it seems that bioprospecting, with its potential as a rich and important source of new therapeutic leads for drug research and discovery, is here to stay. Collaborations between pharmaceutical companies and the countries supplying the indigenous knowledge and medicinal resources could offer an important new revenue source for impoverished developing countries; however, future bioprospecting endeavors will require sensitive handling to avoid accusations that Western drug companies are plundering indigenous knowledge. Therefore, efforts to establish fair and equitable partnerships between the pharmaceutical industry and the developing countries are imperative to ensure sustainable, mutually beneficial relationships.

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