THE VALUE OF UNDISCOVERED PHARMACEUTICALS IN TROPICAL FORESTS[1]

ROBERT MENDELSOHN AND MICHAEL J. BALICK

Mendelsohn, Robert *(Yale School of Forestry and Environmental Studies, 360 Prospect Street, New Haven CT 06511, USA) and* **Michael J. Balick** *(Institute of Economic Botany, The New York Botanical Garden, Bronx, NY 10458, USA).* THE VALUE OF UNDISCOVERED PHARMACEUTICALS IN TROPICAL FORESTS. *Economic Botany 49(2):223–228. 1995. Previous estimates of the potential value of higher plants in tropical forests for pharmaceuticals are too high because analysts mistakenly used gross revenues to value drugs instead of net revenues. Correcting this error, we estimate each new drug is worth an average $94 million to a private drug company and $449 million to society as a whole. Given recent experience searching for new drugs, we estimate that the higher plants in the world's tropical forests contain about 375 potential pharmaceuticals of which 48 (about one in eight) have already been discovered. Multiplying these values by the number of potential new drugs suggests that a complete collection and screening of all tropical plant species should be worth about $3–4 billion to a private pharmaceutical company and as much as $147 billion to society as a whole.*

Key Words: pharmaceuticals; tropical forests; conservation; valuation.

In order to slow the rapid destruction of tropical forests and the concurrent loss of biodiversity, it is critical to identify and quantify the benefits of conserving the remaining standing forests. Although the standing forest provides many market and nonmarket services, including the materials for traditional medicines (Balick and Mendelsohn 1992), the existence of undiscovered pharmaceuticals for modern medicine has often been cited as one of the most important reasons to protect tropical forests (Abelson 1990; Oldfield 1989) and plants in general (Duke 1987; Farnsworth and Soejarto 1985). For example, Gentry (1993) suggests drugs in tropical forests are worth $900 billion and Pearce and Puroshothaman (1993) support a value of $420 billion. Both estimates rely upon a top-down view of the pharmaceutical industry. In this paper, we construct an estimate from the bottom-up, exploring the costs and revenues of developing a new drug from tropical plants. We explore the value of plants from the perspective of a private drug company and society as a whole. Both perspectives are relevant depending upon the property rights and institutions which are established to develop new drugs from plants. Forty-seven major drugs have come from tropical plants to date (Soejarto and Farnsworth 1989). In this analysis, we estimate how many drugs remain to be found and how valuable these drugs are likely to be.

THE NUMBER OF UNDISCOVERED DRUGS

Approximately one-half or 125 000 of the world's flowering plant species live in tropical forests (World Conservation Monitoring Centre 1992). From many species, one can collect five different parts of the plant: roots, stems, leaves, flowers, and fruit. From other plants, only a few parts are available. In addition, one can treat each of these parts to alternative solvents in order to extract chemical compounds. Of course, some of the compounds will be present in more than one part of the plant. We estimate that there are, on average, three distinct parts and two different extraction procedures for each species yielding an average of six different extracts per species. Multiplying the number of extracts by the number of species suggests there are about 750 000 potential extracts which could be obtained from the higher plants in the world's tropical forests.

[1] Received 8 August 1994; accepted 15 February 1995.

There are approximately 500 screens at any one time which could be run on each sample to test for new drugs, according to several colleagues in the pharmaceutical industry who were interviewed (but chose not to be identified). If samples were shared across companies, there could be as many as 375 million (500 screens × 750 000 extracts) individual tests from tropical forest plants. Each major drug company, however, has access to only 50 to 75 screens. From the perspective of any one company, the entire forest would yield only 38–56 million (50 × 750 000 to 75 × 750 000) individual tests.

Experience with large samples of botanical tests over the last two decades suggests that between one in 50 000 and one in a million tests result in viable commercial drugs (Reid 1993; G. Cragg pers.comm.; and A.D. Kinghorn pers.comm.). We conservatively assume the lower success rate for the full population of plants of one per million. Applying this success rate to the total potential number of tests suggests there are about 375 (375 million tests × one per million success rate) potential drugs in tropical forests. With its limited number of screens, an individual company could probably locate only between 38 to 56 (38 million × one per million to 56 million × one per million) of these drugs if it examined all 125 000 flowering plant species.

Altogether there are 47 drugs which have already been discovered from tropical forests including vincristine, vinblastine, curare, quinine, codeine, and pilocarpine (Soejarto and Farnsworth 1989). Given our estimate that there are about 375 total drugs in the forest, scientists have discovered 12.5% or one in eight of these drugs to date. Approximately 328 drugs remain "hidden" in tropical forests at present. Given the assumptions listed above, a private company could expect to find between 33 to 49 of these new drugs if the entire resource was examined.

The Value of an Undiscovered Drug

Many of the detailed facts used in the following analysis were gathered in a recent study by the Office of Technology Assessment (OTA 1993). Out-of-pocket research and development expenses increased from $65 to $155 million per successful drug between the 1970's and 1980's (Hansen 1979; DiMasi, Bryant, and Lasagna 1991). These costs include the many false leads from drugs which do not pass all preclinical and clinical trials. Drug development, including clinical trials, takes an average from 9 to 12 years from start to FDA approval for sale. Companies spend about $155 million over this initial ten year period bringing a drug to market. Using a five percent real (inflation removed) interest rate, the present value of research and development costs per successful drug is about $125 million.

Grabowski and Vernon (1990) demonstrate that the sales revenues from new drugs follow a hill-like pattern for a company, peaking 10 years after FDA approval for sale and declining thereafter. The sales value at the peak has been increasing over time, moving from about $50 million for new drugs in the 1970's to $150 million for new drugs in the 1980's. After loss of patent protection, sales revenues for the original company erode with the advent of generic competition. The sales distribution over time is presented in Table 1.

The OTA study identifies several expenses incurred to generate the sales reported in Table 1. First, a facility must be developed to produce the drug. The average cost of a facility is about $25 million. The annual cost of this capital expense is about $1.25 million per year (at a five percent interest rate). Second, there are manufacturing costs equal to about 25.5% of sales which include maintenance, depreciation, labor, and material expenditures. Third, there are marketing and administrative costs, which equal about 33.6% of revenues over the product's lifetime. Fourth, there are inventory and account receivable costs which amount to 1.5% of sales. Finally, there are ongoing research and development costs associated with expanding the potential market for the drug. These expenditures average $3.14 million per year over the first nine years in which the drug is sold as shown in Table 1.

Subtracting costs from revenues yields a stream of profits or net revenue per year for 20 years. Discounting this stream back to the year the plant sample is delivered yields a net present value of about $125 million per drug to a private firm. Assuming that companies pay average taxes of about 25% on profits, the after-tax value of a new drug to a private company is about $94 million. Given uncertainty about the timing, cost, and magnitude of sales, the standard error around this estimate is about $50 million. Our $94 million estimate is significantly higher than the OTA estimate of $36 million because their study uses a 10% nominal interest rate instead of a 5% real

TABLE 1. ANNUAL PRIVATE COSTS AND REVENUES ASSOCIATED WITH A NEW DRUG.[1]

Year	R&D costs	Production costs	Sales revenue	Net revenue	Cumulative net present value
1–10	15.5	0	0	−15.5	−125.0
11	3.1	13.4	20	3.5	−122.9
13	3.1	46.7	75	25.2	−92.6
15	3.1	64.9	105	37.0	−59.6
17	3.1	80.0	130	46.9	−20.1
19	3.1	92.2	150	54.7	22.0
21	0	74.0	120	46.0	59.5
23	0	61.9	100	38.1	85.6
25	0	50.0	80	30.0	104.6
27	0	34.6	55	20.4	117.0
29	0	16.4	25	8.6	122.6

[1] All amounts are in millions of dollars with only odd years shown. Sales are assumed to begin in the tenth year of development. Figures are adapted from OTA (1993) using a 5% interest rate.

interest rate. Given that inflation has been removed from their report and ours, the real (inflation-adjusted) interest rate of 5% should be used.

If a private company were given the rights to develop all the drugs from tropical forests, the gross revenue from each potential drug would be worth approximately $96 million. As discussed in the earlier section, a single company should expect to find between 33 to 49 new drugs if it examined all tropical plants. Multiplying the number of drugs times their individual value, the company should expect gross revenues of $3.2–4.7 billion (33 to 49 × $96 million). Assuming that the desired samples from across the world could be collected at an average cost of $100 each, collection costs would amount to $75 million (750 000 samples × $100). Assuming that test screens cost another $100 each adds an additional expense of $360–530 million ($100 per test × 36 million tests to $100 × 53 million). The net revenue from the right to the forest is the gross revenue minus costs, $2.8 to 4.1 billion ($3200 − $75 − $360 million to $4700 − $75 − $530 million). The earth contains approximately 3.1 billion hectares of tropical forest (Sharma et al. 1992). If net revenues were allocated equally to every forest owner by hectare, the payment would amount to $.90–$1.32 ($2.8 to $4.1 billion/3.1 billion hectares) per hectare.

If the same issue is viewed from a collective perspective, the drug value is much higher. First, if the plant extracts are shared among drug companies, more screens can be utilized which will result in more drugs being found. Second, collective drug sales are not expected to decline after 10 years. The "hill-like" path of profits over time for an individual company occurs because patent protection runs out in ten years and generic sales replace patent sales. However, if one was simply measuring aggregate sales (across all companies), peak net revenues, $58 million, are likely to be maintained indefinitely. Third, from a social perspective, revenues lost to taxes are not lost to society. Returning to Table 1, the social net present value of a drug for its first 19 years of development would be worth $22 million. Beyond 20 years it would continue to earn $58 million per year which has a net present value of $422 million (exp(−.05 × 20) × $58 million per year/.05). Adding these figures together yields a total value of $449 million per drug. The aggregate potential social value for undiscovered tropical forest pharmaceuticals is about $147 billion ($449 million per drug × 328). Allocating this aggregate net value per hectare yields an average payment of $48 per hectare.

CONSERVATION AND UNDISCOVERED DRUGS

This paper draws the link between potential drugs and tropical forest conservation by quantifying what is known about these undiscovered drugs. Although many of the parameters required to make this link are uncertain, the analysis is able to provide an estimate of the magnitude of potential drug development in tropical forests. We estimate that the full potential social value of undiscovered drugs is about $147 billion or about $48 per hectare. In contrast, the market value of what an individual drug company should pay for the right to the remaining drugs hidden in the world's tropical forests is closer to $3–4 billion or about $1 per hectare.

In order to secure the potential value from hidden drugs in the tropical forest, a number of hurdles must be overcome. First, it must be established who can purchase genetic material. Second, it must be established who can sell genetic material. Depending upon how these two issues are handled, the financial incentive that hidden drugs contribute to preserving tropical forest can vary from zero to $147 billion.

The first task listed above is to decide on a mechanism for purchasing genetic material. In the absence of a mechanism, anyone can purchase a sample from the forest but no one has exclusive rights to a species or type of sample. Companies are free to collect as many samples as they wish but they cannot prevent other companies from examining the same materials. In this setting, companies will compete to discover drugs and may explore identical plants. Since the first one to discover a useful compound can gain rights over the drug, companies must weigh their likelihood of not only finding a successful sample but also finding it first. This reduces their incentive to invest in drug development and will lower what they would pay for a drug below the potential value of a drug to a private company.

The transaction value for bioprospecting in the tropical forest would probably be higher if purchasers were able to obtain exclusive rights to plant materials. With exclusive rights, the company would be free to invest in drug development without being concerned that another company was following the identical path. The problem with granting exclusive rights to any one company is that they do not have access to all the screens that can be run on a sample and their private rewards for finding the drugs falls well below social incentives. We estimate that a new drug is worth only $96 million to a company whereas it is worth approximately $450 million to society.

For example, Costa Rica, with its abundance of tropical ecosystems, has an unusually large number of tropical plant species and therefore a high potential for harboring undiscovered drugs. Costa Rica's 1.8 million hectares of tropical forest contain about 7260 species of higher plants (calculated as ⅔ of the mean of the 10 000–12 000 plant species projected to be in the country (World Conservation Monitoring Centre 1992)). These 7260 species comprise about 5.8% of the world's tropical forest species of higher plants. With 5.8% of the species, Costa Rica should have 5.8% of the undiscovered drugs in all tropical forests. Suppose that Costa Rica made a private agreement with a single company to co-develop all the "hidden" drugs within its forests. The private company, with their limited screens, would expect to find between 2 to 3 drugs (5.8% of 33 to 49). Given a net value of $94 million per drug, this arrangement would be worth between $192 to $288 million. If all the profits were allocated to the landowners of Costa Rica, the financial incentive to protect the forest would be $10 to $16 per hectare ($192 to $288 million/1.8 million hectares). Of course, once the forest is tested for its potential drug values, this incentive would become minimal.

Because the collective value of samples far exceeds the private market value, it is tempting to try to create a public organization that collects samples and provides them to drug companies. By allocating the samples across companies, more screens can be employed which will increase the number of potential drugs found. However, obtaining the maximum public value of genetic resources may be quite difficult. First, by handing out samples to many companies, there could be excessive duplication of research and development costs. Care would have to be taken in allocating the drugs among companies to reduce the chance that more than one company is following an identical development path. Second, the drug companies might need to be subsidized, for example by providing tax breaks on research and development, in order to give sufficient financial incentives to find all the new drugs. Third, cumulative experiences with public entities suggest they become inefficient over time and subject to political interests that would affect performance.

The second hurdle which needs to be overcome concerns who can sell genetic material. At the moment, any owner of a plant can sell a sample to a drug company. All the other owners of that same plant receive nothing. The other owners consequently have an incentive to compete with the first owner and be the only person receiving a payment. This kind of competition will drive the resource value to zero. In order for the market for potential drugs to have maximum positive impact on conservation, the financial gain from developing drugs from a given species must belong to all owners of the species. Whether this value is simply shared equally by all owners, shared in proportion to the number of hectares of the plant, or shared in proportion to the population of the plant, some sharing mechanism must be developed for such use of genetic materials. Without a sharing mechanism, there may still be an incentive for drug companies to develop as yet undiscovered drugs from plants, but there will be no reason for the companies to share the resulting profits with landowners. For example, in the absence of an international agreement concerning genetic rights with the current unstructured arrangement, potential drug development provides no incentive to conserve the forest since forest owners get almost none of the potential profits from new drugs.

Another important assumption in this paper is that the undiscovered drugs would have the same average value as recent drugs. Many of the potential drugs could duplicate existing drugs and have much lower added value. Partly because it is harder to find new drugs, research and development costs per successful new drug should rise over time, which would also lower net values. On the other hand, the demand for pharmaceuticals has been expanding rapidly, resulting in growing sales revenues over time. This is likely to continue as international demand increases with economic and population growth. Medical science has also been expanding the number of screens for drugs over time and the treatments for which drugs are effective, which increase the expected value of drugs. These various forces counterbalance each other suggesting that the estimates in this paper are unbiased although highly uncertain.

Comparing our aggregate estimate with the top-down approaches from the literature reveals that the previous literature overestimated the social value of undiscovered drugs by a factor of 2–6 times by underestimating the costs of development and production. These social values, in turn, overestimate market values by about two orders of magnitude because individual companies have limited screens (and so cannot find all the drugs), limited patents (and so cannot collect all the potential revenue), and must pay taxes (which reduces their incentive to find new drugs).

The literature on drug development reveals that developing new drugs is expensive. The average successful drug costs about $125 million to find and develop. This is a sizable investment for a developing country, given both the risk and the long development period. For example, the research and development costs required to find and develop the 19 expected drugs from higher plants in the Costa Rican forest would require an expenditure of $2.4 billion, but the entire GNP of Costa Rica was only $4.9 billion in 1989 (Sharma et al. 1992). It is probably not practical to expect the governmental and nongovernmental institutions of small developing countries to independently develop their own drugs. Instead, these institutions may find it more attractive to form partnerships with large pharmaceutical companies, combining the traditional knowledge, natural resources, taxonomic expertise, and labor of one with the capital, research, and marketing strengths of the other.

Concerns for biodiversity, ecosystem function, and global warming have proven to be important motivations for tropical forest conservation. Market products and services provide additional quantifiable reasons to preserve standing forests. Extraction of non-timber forest products (Balick and Mendelsohn 1992; Grimes et al. 1994; and Peters, Gentry, and Mendelsohn 1989) and tourism (Tobias and Mendelsohn 1991; Maille and Mendelsohn 1993) are both economically competitive and viable activities in selected natural forests. This article provides quantitive evidence of yet another reason to slow deforestation and preserve biological diversity. The potential value of undiscovered drugs is an additional incentive to conserve species-rich forests throughout the world. If the property rights to these resources can be established, as yet undiscovered drugs will become another powerful financial incentive to conserve tropical forests.

Acknowledgments

We would like to thank Scott Mori, Lynn Caporale, Douglas Daly, Sarah Laird, A. Douglas Kinghorn, Gordon Cragg, Georg Albers-Schonberg, and W. Nordhaus for their valuable assistance in preparing this paper.

Literature Cited

Abelson, P. H. 1990. Medicine from plants. Science 247:513.

Balick, M., and R. Mendelsohn. 1992. The economic value of traditional medicine from tropical rain forests. Conservation Biology 6:128–139.

DiMasi, J., N. Bryant, and L. Lasagna. 1991. New drug development in the United States, 1963–1990. Clinical Pharmaceutical Therapeutics 50:471–486.

Duke, J. 1987. Economic impact of botanicals. Pages 1–5 *in* L. Grant, ed., Proceedings of second national herb growing and marketing conference. Purdue Research Foundation, W. Lafayette, IN.

Farnsworth, N., and D. Soejarto. 1985. Potential consequences of plant extinction in the United States on the current and future availability of prescription drugs. Economic Botany 39:231–240.

Gentry, A. 1993. Tropical forest biodiversity and the potential for new medicinal plants. Pages 13–24 *in* A. D. Kinghorn and M. F. Balandrin, eds., Human medicinal agents from plants. American Chemical Society, Washington, D.C.

Grabowski, M., and J. Vernon. 1990. A new look at the returns and risks to pharmaceutical R&D. Management Science 36:804–821.

Grimes A., S. Loomis, P. Jahnige, M. Burnham, K. Onthank, R. Alarcon, W. Palacios Cuenca, C. C. Martinez, D. Neill, M. Balick, B. Bennett, and R. Mendelsohn. 1994. The value of tropical forests: a study of nontimber forest products in the primary forest of the Upper Napo Province, Ecuador. Ambio 23:405–410.

Hansen, R. 1979. The pharmaceutical development process: estimates of development costs and times and the effect of proposed regulatory changes. Pages 151–191 *in* R. Chien, ed., Issues in pharmaceutical economics. DC Heath Co., Lexington, MA.

Maille, P., and R. Mendelsohn. 1993. Valuing ecotourism in Madagascar. Journal of Environmental Management 39:213–218.

OTA (Office of Technology Assessment). 1993. Pharmaceutical R&D: costs, risks and rewards, U.S. Government Printing Office, Washington, D.C.

Oldfield, M. L. 1989. The value of conserving genetic resources. Sinauer Associates, Sunderland, MA.

Pearce, D., and S. Puroshothaman. 1993. Protecting biological diversity: the economic value of pharmaceutical plants. CSERGE, University College, London.

Peters, C., A. Gentry, and R. Mendelsohn. 1989. Valuation of an Amazonian rainforest. Nature 339: 655–656.

Reid, W. V. 1993. A new lease on life. Pages 1–52 *in* W. V. Reid, S. A. Laird, C. A. Meyer, R. Gamez, A. Sittenfeld, D. H. Janzen, M. A. Gollin, and C. Juma, eds., Biodiversity prospecting: using genetic resources for sustainable development. World Resources Institute, Washington, D. C.

Sharma, N., R. Rowe, K. Openshaw, and M. Jacobson. 1992. World forests in perspective. Pages 17–31 *in* N. Sharma, ed., Managing the world's forests. Kendall/Hunt Publishing Company, Dubuque, IA.

Soejarto, D., and N. Farnsworth. 1989. Tropical rain forests: potential source of new drugs? Perspectives in Biology and Medicine 32:244–256.

Tobias, D., and R. Mendelsohn. 1991. Valuing ecotourism at a tropical rain forest preserve. Ambio 20:91–93.

World Conservation Monitoring Centre. 1992. Global biodiversity: status of the earth's living resources. Chapman and Hall, London.