The economic value of plant-based pharmaceuticals

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Introduction

There is increasing recognition that the economic rate of return to sustainable forms of natural resource use is both positive and capable of exceeding the returns to alternative forms of land use, such as agriculture and clear-felling for timber (Peters et al., 1989; Swanson and Barbier, 1992; Pearce and Moran, 1994). Where the rate of return analysis does favour the conservation of biological resources and biological diversity, the requisite land use will still not be realised if either: (1) the benefits of conservation have no marketable dimension (a form of ‘market failure’), or (2) governments intervene in the market place to distort economic signals in favour of exploitative land use that involves biodiversity loss. Clearly, then, two stages in the economic case for biodiversity conservation are: (1) demonstrating the economic value of biodiversity conservation, and (2) implementing mechanisms whereby those values can be appropriated and captured. We refer to these stages as the demonstration and appropriation stages in the process of conserving biodiversity.

This paper is concerned with the first stage of the argument: demonstration. It is concerned, moreover, with only one aspect of economic value: the form of use value reflected in the actual or potential and direct application of plants in the production of pharmaceuticals. To narrow the focus even further, we concentrate on the global commercial value of medicinal plants, by which we mean the potential for commercial use outside of what is typically known as ‘traditional medicine’. This should not be taken to imply that traditional medicinal uses are without economic value. Indeed, such values may be large (Balick and Mendelsohn, 1992). Other use values, for example eco-tourism, may also be important, whereas non-use values (‘existence’ and ‘bequest’ values) may be more important still (Pearce and Moran, 1994). The process of demonstrating economic value, however,
only really commenced in the last few years and it is important to build up the component parts of value. Finally, the focus on economic value does not mean that other value concepts are not relevant (see the survey on values by Swanson, this volume), nor do the economic values discussed here claim to be necessarily comprehensive. Bateman and Turner (1993), for example, suggest that there is a prior concept of economic value, 'primary value', on which all the economic values discussed here depend. Primary value is best thought of as some kind of 'life support' value.

**Plants and medicine**

Plant species are used for medicines in two ways: (1) as a major commercial use, whether by prescription or over-the-counter sales, and (2) as traditional medicines which may or may not attract a market price. In the rich world, perhaps 25% of all medical drugs are 'based' directly on plants and plant derivatives; this means that they remain linked directly to those plant forms for their production. In the poor world the proportion of drugs based on plants is closer to 75% (Principe, 1991). Clearly, both uses have an economic value.

Of course, most of the contributions of plants to the production of pharmaceuticals do not rely on their direct utilisation in production processes; they contribute instead by means of providing 'leads' or 'targets' which then serve as the foundation for future synthesis of a drug. Whereas some useful chemical compounds discovered within medicinal plants have not been reproduced synthetically (digitoxin, for example), and others have been reproduced but are less efficient than the original material (for example synthetic vincristine from *Catharanthus*), in most cases synthetic substitutes do exist. Therefore, the estimation of the value of plant-based pharmaceuticals clearly represents an attempt to value only a small subset of the total value of plant diversity for its contribution to the pharmaceutical industry.

This estimate of the value of plant-based pharmaceuticals is, in one sense, a serious underestimate of the total value. In another sense, however, it may be a serious overestimate on account of the problematic nature of using past and present usage as an indicator of future uses. The important issue here is: Are future drugs more, or less likely to be manufactured from plant-based materials? The answer to that question has been addressed elsewhere in this volume (see Aylward and Albers-Schonberg). Here, the economic literature on this question is surveyed.

Principe (1989) reports on a UN International Trade Centre study which suggests that, during the 1970s and early 1980s, pharmaceutical
companies showed a decreasing interest in the development of new botanical products in favour of molecular biology and biotechnology applications to microorganisms. Processing plant genetic material is time-consuming and expensive, and simple comparative rates of return are higher from other routes. On the other hand, others in the industry appear to believe that plant-based resources will re-emerge, and one company, Merck, has entered into a licence and royalty agreement with Costa Rica. Merck's example does not appear to have been followed by any other company, but there are signs of a revived interest in plant material for drug development.

Principe (1989) reports several reasons why research based on microorganisms has limitations. The most important are: (1) the steps of identifying the chemical structure required to achieve a given effect and creating a proper genetic code structure are the most difficult stages of drug development, and these are not helped by microorganisms rather than plant-based genetic material, and (2) genetically engineered microorganisms can, so far, substitute for only some of the plant-based chemicals. Indeed, Principe reports that the vast majority of plant-based chemicals have not been successfully synthesised.

The future of drug development may also be more, rather than less, dependent on plant genetic material in light of the fact that plant-based research has gone in cycles. Findeisen (1991) reports that many thought that plant-based drug resources were exhausted in the early part of this century. The role of plants was, however, revived in the 1940s and 1950s with the discovery of the Vinca alkaloids (*Catharanthus rosea*) and reserpine (*Rauwolfia serpentina*). When the screening programmes at the National Cancer Institute (NCI) and elsewhere in industry failed to come up with significant discoveries, the industry lost interest and screening programmes were effectively halted in the 1970s. The disinterest was compounded by the difficulties of plant-based drug patents that have to relate to the process of manufacture or to some unanticipated use value. Natural compounds *per se* cannot be patented (see Walden, this volume). Thus, the Mexican government took control of Diosgenin resources in order to capture the rent from the production of *Dioscorea*, the main source of steroids in the early days of that drug. Attempts at the monopoly pricing of the resource forced pharmaceutical companies to search for synthetic substitutes. The case illustrates the problems of patenting and the problems facing countries that do seek to capture rents from biodiversity.

Some revival of interest in plant-based approaches in the last 5 years is accounted for by new techniques of purifying, analysing and assaying plant samples, including the use of robots for continuous assay of material. It is
reported that the NCI, Monsanto, Smith Kline, Merck and Glaxo have revived plant screening programmes. Affymax and Shaman are new companies in the USA developing drugs solely from natural products, and with a lot of emphasis on traditional medicines. The other main source of a revival in interest in medicinal plants is consumer demand for 'natural products'. While consumers are unlikely to express a concern about the source material for major life-saving drugs, they do express a significant concern about the sources of over-the-counter drugs and cosmetics, as the success of some natural products shops reveals.

Clearly then, medicinal plant values are relevant to use value arguments for conserving biological resources, especially in the developing world. How far they have relevance in justifying conservation of biodiversity as such is more of a problem. Some commercial sources doubt that genetic engineering of microorganisms will totally displace plant-based research. This would suggest an insurance argument for conserving at least minimum diversity based on arguments related to the option values of the resource (see Swanson, this volume). These arguments are all the more powerful because of the extremely limited knowledge that exists about the medicinal properties of plants.

Evenson (1990) addresses these questions to an extent. He distinguishes between two fundamental values of genetic resources as producer goods: one in the general strategic search for new resources which justifies the maintenance of most materials, and another in the specialised search for genetic material to meet specific needs, which justifies the collection and preservation of 'fringe' genetic resources. His calculations for rice suggests that if there is an economic case for maintaining an ex-situ collection, the case for maintaining a near complete collection is stronger.

Overall, then, the economic value to medicinal plants falls into two general categories, one readily estimated and the other not. The first relates to the use values of plant-based drugs. These are drugs that remain closely connected to the plant form from which they were derived, and there exists a significant market in the drug; this value is appropriable and readily estimated. The other contribution of medicinal plants to the pharmaceutical industry is much more general and amorphous; it is the value of providing 'leads' in the creation of ultimately synthesised pharmaceuticals. This value is 'informational' in nature, and is very difficult to appropriate and to estimate. It is not the subject of this chapter. Here we attempt to provide a concrete estimate of the clearly attributable value generated by medicinal plants in the pharmaceutical industry. It is a 'floor' to the valuation of biodiversity, on which other values of diversity may then be constructed.
The economic value of plant-based drugs

Ideally, what is required for economic valuation purposes is some idea of the ruling prices for plant genetic material and elasticities of demand by drug companies for that material. Given the availability of synthetic substitution as an alternative technology for some drugs, it seems clear that the demand elasticity will be high for those drugs, but fairly low for plant-based material that cannot, so far anyway, be synthesised. Drug companies today tend to use specialist plant gathering agencies (botanical gardens in USA and a private company, Biotics, in the UK). In turn the gathering agencies use local institutions and people to engage in actual collection and shipping. Payment to the gathering companies is by contract or weight of material, but there are examples of agreements involving royalties in the event of successful exploitation. Thus, Biotics has royalty agreements with the companies it supplies and, in turn, those royalties are divided between the company and the source countries. To this end, these agreements already provide for the sharing of rents in the way clearly intended by the Biodiversity Convention negotiated at the Earth Summit conference in Rio in 1992. Findeisen (1991) reports that royalties are usually negotiated on the basis of the value of the drug to the drug company, with royalty figures being in the range 5–20%. Royalties, however, are more readily negotiated for plant material to be used in a drug that is near to being marketed. Material that is destined for screening for longer term development is likely to attract low royalty agreements or simple once-off fees. Other companies have straight retainer agreements with botanical gardens and no royalty agreements. In the model used later, we therefore assume that a royalty rate of 5% is applied to any plant material that results in the development of a successful drug.

Economic valuation to date has been fairly speculative but illustrative of the orders of magnitude involved (Farnsworth and Soejarto, 1985; Farnsworth et al., 1985; Principe, 1989, 1991). There are several ways in which to approach valuation:

1. by looking at the actual market value of the plants when traded;
2. by looking at the market value of the drugs of which they are the source material;
3. by looking at the value of the drugs in terms of their life-saving properties, and using a value of a 'statistical life'.

If we do not take into account the prevailing institutional capability to capture the values in discoveries as implied in 2 and 3, the result will be
exaggerated valuations for the host country. As Ruitenbeek (1989) notes, the economics of invention reveals that income realized by inventors is considerably less than the ultimate value to society of the product, because the traits associated with the ultimate products have a very low degree of appropriability. This is true with respect to the countries providing niches to the diverse flora and fauna where the discoveries have to be made. This aberration in rent appropriation becomes even more blurred when the assumptions of ignorance, uncertainty, essentiality and substitutability about medicinal plants enter the analysis. This implies that a factor representing the institutional framework should be applied to the ex-post discovery valuation. This factor will depend on the existence of the licensing structure in the host countries; whether research conducted in the host country causes other leakages in the economy; and whether the ability exists domestically to carry out the research. Thus this factor is expected to be low in tropical low income economies. In Ruitenbeek's terms:

\[ CPV = a \times EPV, \]

where CPV is capturable production value, EPV is expected production value, that is the patent value of one discovery. The fact that \( a \) tends to be low explains why developing nations feel that the benefits of their efforts to conserve biodiversity is captured more by others, that is, \( a \) can be thought of as a coefficient of rent capture. One purpose of the Rio Biodiversity Convention is to raise the value of \( a \).

A model of economic valuation of medicinal plants

We are now in a position to develop a simple model for determining the medicinal plant value of a unit of land as biodiversity support. The approach is fraught with difficulties given the considerable data deficiencies, but it is worth pursuing.

For any given area, say a hectare, there will be some probability, \( p \), that the biodiversity 'supported' be that land will yield a successful plant-based drug \( D \). Let the value of this drug be \( V_i(D) \), where subscript \( i \) indicates one of two ways of estimating the value: the market price of the drug on the world market \((i = 1)\), or the 'shadow' value of the drug which is determined by the number of lives that the drug saves and the value of a statistical life \((i = 2)\). As there are many other factors of production producing value in the drug, let \( r \) be the royalty that could be commanded if the host country could capture all the royalty value attributable to natural capital. Finally, let \( a \) be the coefficient of rent capture discussed previously. Then, the medicinal plant value of a hectare of 'biodiversity land' is:
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\[ V_{mp}(L) = p \times r \times a \times V_i(D). \]

We consider each element of this equation in turn.

**Probability of success**

Prínципe (1991) estimates that the probability of any given plant species giving rise to a successful plant-based drug is between 1 in 10,000 and 1 in 1,000. These estimates are based on discussions with drug company experts. Of course, the probability of success is closely linked to the information used in the process of screening the plants (see Balick and Fellows, this volume), but here we are abstracting from the role of information and looking only at the contribution of the chemical structures within the plant itself. For our purposes it will be assumed that plants are screened randomly and that the above figures are reasonable estimates of the range of probabilities for the derivation of a plant-based drug from the screening of these plants.

Estimates of the number of plant species likely to be extinct in the next 50 years or so vary, but a figure of 60,000 is widely quoted (Raven, 1988). This suggests that somewhere between six and 60 of these species could have significant plant-based drug values. Put another way, if biodiversity use were favoured over alternative land uses, the realised benefit as far as plant-based drugs are concerned would be the economic value of these six to 60 species.

**The royalty**

Existing royalty agreements involve royalties of 5–20%, but are primarily at the low end of that spectrum at present. Of course, royalties are a function of the property rights system in effect, and therefore could vary substantially with different systems. Here, however, the royalty is assumed to represent the ‘marginal product’ of the plant’s contribution to the value of the plant-based drug (relative to the other factors of production: labour, capital), and in the absence of other information the current royalty rate will be used.

**Rent capture**

If host countries could capture rents perfectly then \( a = 1 \). Ruitenbeck (1989) suggests that rent capture is likely to be as low as 10% in low income
countries. Hence a range for $a$ is $a = 0.1$ to $1.0$. To some extent, this concept is not distinct from the issue of ‘royalty’ rates, but it may be so when there are two distinct entities involved in: (1) providing the habitat to explore, and (2) providing the expertise for the exploration. Then rent capture would accord with the return to the party providing the natural habitat and the royalty would accord with the return to the other factors of production (labour, skills) used in its exploration. Here we will collapse the two elements together by assuming that royalties are fixed in accordance with the marginal product of plants in the production of pharmaceuticals (at around 5%) whereas the providers of the medicinal plants appropriate a return (of between 10 and 100% of the royalties paid) representing a joint return on the habitat provided and the skills utilised in exploring it. This seems to accord best with current realities, but these realities (it is important to keep in mind) are determined by current property right entitlements.

The value of drugs

Table 6.1 adapts work by Principe (1989, 1991) and summarises some estimates of the value of successful plant-based drugs. The method of valuation is important because it affects the size of the estimate significantly. The valuation based on life-saving properties gives the highest values, using the value of a ‘statistical life’ of $4$ million (Pearce et al., 1992). The market values of plant-based drugs give lower values, and the actual trade price of the plant material the lowest value of all.

The price of drugs reflects, of course, many more things than the cost of the plant source material. In that respect, the drug price grossly overstates the value of the plant; however, as indicated above, the contributions of the other factors of production in the creation of pharmaceutical value is taken into consideration in the analysis of the effects of various ‘royalty rates’.

In fact, market prices will actually understate true willingness to pay for drugs: there will be individuals who are willing to pay more than the market price for a given drug. Indeed, because the evidence suggests that such drugs tend to be price inelastic, this ‘consumer surplus’ element could be substantial. This consumer surplus is another element of value that would have to be built upon the foundation figure that we are developing here.

Now we introduce an indicator of just how limiting is our estimation of the contribution of plants to the pharmaceutical industry. In the 1980s only about 40 plant species accounted for the plant-based prescribed drug sales in the USA; despite the wide range of contributions of plant communities to medicinal knowledge worldwide, our analysis focuses solely on the value
Value of plant-based pharmaceuticals

Table 6.1. The value of plant-based drugs

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<td>Market value of medicinal plants</td>
<td>5.7</td>
<td>17.2</td>
<td>24.4?</td>
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<tr>
<td>Market or fixed value of plant-based</td>
<td>11.7</td>
<td>35.1</td>
<td>49.8?</td>
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<td>drugs on prescription</td>
<td>15.5</td>
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<td>(1985)</td>
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<td>19.8</td>
<td>59.4</td>
<td>84.3?</td>
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<td>Value of plant-based drugs</td>
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<td>based on avoided deaths</td>
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<td>Anti-cancer only</td>
<td>120.0</td>
<td>360.0</td>
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<td>Non-cancers</td>
<td>240.0</td>
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a$ billion 1990 prices.

The year in parentheses refers to year of estimate.

The ratio of OECD to USA taken to be 3. 'Value of a statistical life' taken to be $4 million at 1990 prices. Lives saved taken to be 22,500-37,500 per annum in USA. The average is taken here, i.e. 30,000. Multiply OECD by 1.4 to obtain world estimates.

Source: adapted with modifications from Principe (1989); see also Principe (1991).

of the contributions of these 40 species. Thus, on the basis of prescription values only (Table 6.1), each species was responsible for $11.7 billion/40 = $290 million on average. As all life-saving drugs would be on prescription, use of the value of avoided deaths suggests a value per plant of $240 billion/40 = $6 billion per annum. Clearly, some species were far more valuable than others but, taking the average, it is possible to get some idea of the lost pharmaceutical value from disappearing species. If there are 60,000 species likely to be unavailable for medical research, and the probability that any given plant will produce a marketable prescription drug is $10^{-3}$ to $10^{-4}$, then taking a mean of $5 \times 10^{-4}$ and applying it to the 60,000 estimated losses means that 30 plant-based drugs will be lost from species reduction. On market-based figures, the annual loss to the USA alone would therefore be 30 x $292 million = $8.8 billion, and to Organisation for Economic Cooperation and Development (OECD) countries generally perhaps $25 billion. Principe (1991) suggests that in the USA in
1990, prescription plant-based medicines had a retail value of $15.5 billion, which would raise the value per plant to $390 million. As a benchmark, the Gross National Product (GNP) produced in the whole of Brazilian Amazonia is some $18 billion per annum (Gutierrez and Pearce, 1992). On the ‘value of life approach’ the annual losses would be $6 billion = $180 billion for the USA, and over $500 billion for the OECD countries generally. These figures, however, assume that substitutes would not be forthcoming in the event that the plant species did become extinct.

The value of land for medicinal plants

Using the previous estimates it is possible to arrive at an estimate of the value of a ‘representative’ hectare of land. It is not always appropriate to express values in respect of land since it implies that land is the scarce factor of production, and this is often not the case in much of the developing world. None the less, expressing values in ‘per hectare’ terms has become the convention in this kind of analysis and it serves to focus on the underlying choice problem, namely which land use to choose among the available options. The model can now be written:

\[ V_{mp}(L) = \frac{N_R \times p \times r \times a \times V/n}{H} \text{ per annum} \]

where \( N_R \) is the number of plant species at risk, \( n \) is the number of drugs based on plant species, \( H \) is the number of hectares of land likely to support medicinal plants. \( H \) is problematic because it is not entirely clear what area to consider as being most fruitful for tropical plant research. We opt here for the total supply of tropically forested land.

The empirical magnitudes are:

- \( N_R = 60,000 \)
- \( p = 1/10,000 \) to \( 1/1000 \)
- \( r = 0.05 \)
- \( a = 0.1 \) to \( 1 \)
- \( V/n = 0.39 \) to \( 7.00 \) billion US$
- \( H = 1 \) billion hectares, the approximate area of tropical forest left in the world.

The resulting range of values is from $0.01 to $21 ha. If \( a = 1 \) at all times, then the range is $0.1 to $21 ha. Clearly, the lower end of the range is negligible, but the upper end of the range would, for a discount rate of 5% and a long time horizon amount to a present value of some $420 ha.
Other estimates of medicinal plant values

Ruitenbeek (1989) suggests an annual value of $85,000 (£50,000) for a = 1 for the Korup rainforest in the Cameroon. The relevant area is either 126,000 ha (the central protected area) or 426,000 ha (the central area plus the surrounding management area), so that per hectare values would be $0.2 to $0.7 per hectare per annum, very much in keeping with the lower end of the range obtained from our own model.

In an interesting contrast to our analysis, in a study of harvesting of medicinal plants in Belize, Balick and Mendelsohn (1992) estimate the local willingness to pay for land. Their annual net revenues are $19-61 per ha, substantially greater than those derived here. This indicates that the value of any given hectare of land may differ quite markedly from the average (of perhaps $20 per ha), as would be expected. Conservation of this particular value of diversity may be used to generate quite substantial values, not in relation to all of the remaining natural habitat but only with regard to some subset of that.

Conclusion

Overall, then, despite the formidable data problems and the difficulties involved, the model used here does produce a very concrete estimate of the contribution of the global tropical forests to the production of plant-based drugs; this value lies in a range from very low to around $20 per hectare.

These values relate to the species ‘at risk’. Clearly, the actual values must be higher as the loss of very large tracts of tropical forest would place many other plant species at risk. We therefore construe these values as very much lower bounds. This economic value is the foundational element for estimating the total contribution of plant resources to the production of pharmaceuticals. It would be additive with all of the other values that these resources generate, and it would be additive with all of the other contributions that these resources make to the pharmaceutical industry. ‘True’ economic valuations would incorporate a wider range of uses than those estimated here, but this study has focused on the development of a concrete value for one very particular use of biodiversity, namely direct use in plant-based pharmaceuticals.

References


