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PRESERVATION AND UTILIZATION OF NATURAL BIODIVERSITY IN CONTEXT OF SEARCH FOR ECONOMICALLY VALUABLE MEDICINAL BIOTA

(IUPAC Recommendations 1996)

Prepared for publication by

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Preservation and utilization of natural biodiversity in context of search for economically valuable medicinal biota (Technical Report)

Abstract - Natural products remain excellent sources of leads in the search for novel medicaments for the treatment of diseases. The largest present underexplored source of such materials lies in tropical and subtropical regions. In these areas a long tradition of ethnobotanical medicine often exists with which to guide laboratory experimentation, but the finds, equipment and necessary expertise is often lacking. The divergence betwen availability and the means with which to develop provides the basis for significant disagreements over the value to be placed on each party's contribution and represents a factor which inhibits the development of these materials for mankind's benefit. Various scientific societies, governmental agencies, industries, groups and individuals have advanced their views, but confounding features have prevented the emergence of an amicable consensus. The rapid rate with which biota are disappearing has increased the urgency of the need to find solutions to the problems which remain. IUPAC has considered a number of declarations on the subject, particularely the Manila Declaration of 1992 and the Melaka Accord of 1994, which are reproduced in an appendix, and has made several recommendations it believes should be considered by participants when promulgating declarations and enacting legislation on the topic. This position paper sets forth IUPAC's views on the subject for the guidance of its members and affiliated organizations and is not itself a declaration nor does it adopt by reference any particular declaration.

BACKGROUND

In the search for new medications natural products have proven productive sources of leads for centuries and interest in them remains high despite the emergence of several competing modalities for lead substance generation.

The tropical and subtropical regions of the world are presently the most productive regions for exploration and contain the greatest remaining known source of under explored biodiversity. In many of these areas ethnobotanical medicine flourishes and a great wealth of knowledge has built up over the years. In developed nations the contemporary emphasis is primarily on individual pure ingredients. In developing nations an extensive resort to ethnobotanical remedies exists alongside of western medical systems. However, with few exceptions, the most sophisticated technologies for exploring and developing these leads and the largest markets for the sale of the fruits of this work lie outside their boundaries. This divergence between availability and the ability to develop provides a fertile area for differences over the comparative economic value of each other's contribution and has raised practical barriers to scientific progress.

An intense debate is now raging in which passionately held and very diverse opinions are forcefully advanced in an attempt to influence legislation and behavior in the area of intellectual and other property rights in the context of the search for economically valuable biota. Various scientific societies, governments, industries and individuals have advanced their views in an attempt to reach consensus. Unfortunately, overlapping jurisdictions sometimes issue conflicting pronouncements and the possessors of biota and ethnobotanical lore all too often have exaggerated impressions of its economic value whereas those who wish access to these biota and lore have not always valued them appropriately.

Biopreservation is also a critical concern. Biota are being lost at an alarming rate due to pressures of land usage and the practical difficulties of making biopreservation economically attractive. Another contributory factor is the destructive harvesting of biota.

The Convention on Biological Diversity, the Manila Declaration and the Melaka Accord (see Appendix) all address the general subject area of this document.

Following a request from the Australian Academy of Science to endorse the Manila Declaration and the Melaka Accord, IUPAC as a nongovernmental disinterested party among whose accepted missions is facilitation of international cooperation in chemical science, has decided instead to present its own perspective. For the convenience of the reader, the Manila Declaration and the Melaka Accord are attached to this document as an appendix.

ISSUES

Those who live close to nature are often keen observers of its wonders and many currently used medicines, such as morphine and quinine, have resulted from preservation and subsequent investigation of this knowledge. Such knowledge still exists, especially in undisturbed environments. It is obviously potentially valuable but it is a thorny question of what value to place on it. Historically, such knowledge has often been undervalued or uncompensated without any intended ill will. It is recognized that difficulties can develop based on differing social and cultural norms among local populations as compared with firms in developed countries and that more than one local practitioner may be in possession of analogous knowledge of drugs and other useful products passed down for generations.

Where plant or other natural materials are collected for general pharmacological screening, intellectual property rights are clearly less involved. The materials are most sensibly regarded as the property of those having title or jurisdiction to the land upon which they occur subject to the applicable laws of regional, state and national jurisdiction. It is recognized that friction all too often exists between local populations and those claiming authority over them. These problems complicate the issues at hand.

It is a non-trivial question to ask who should benefit from a country's indigenous biota. Ideally those who possess the biota and those who wish to bring its benefits to a wider population should work out equitable and realistic contracts to share in the proceeds according to the intrinsic value they have contributed. It is simplistic to suggest that oil and mineral fields provide an adequate precedent for these resources are not living and cannot multiply. Removal of a few seeds or cuttings of particularly valuable materials can result in enormous value to those effecting the removal and reestablishment at a distant site. This problem is becoming more severe as a consequence of the rapid development of means of transferring genes. Most peoples have until recently regarded genes to be mankind's common heritage. Attempts to patent genetic materials up to and including the human genome and naturally disease resistant plant varieties have changed this view by asserting individual proprietary value to these materials. The providers of genetic material now wish to see their genetic contribution rewarded. The import of this has not been lost to the possessors of a wide variety of genetic materials. It is not possible to construct a parallel scenario in the fields of oil or minerals. In this view bioprospecting is not a comparable term. Constructive approaches to these problems need to be formulated.

Discoveries such as taxol which go unchanged to market are the exception rather than the rule but the problems dealt with above are easier to put in perspective than in the greater majority of cases where the initial discovery is not marketable *per se* but requires extensive chemical manipulation before a marketable version emerges. Those expecting large and immediate financial returns from ethnobotanical discoveries should ponder the reality that it took 30 years from collection to marketing in the taxol case! Cephalosporin C to cefotaxime is a more complex example of this. The initial collection of the mold eventually led to profoundly valuable results, but only after an enormous expenditure of time, ingenuity, and money. Here the initial finding was much less valuable in contributory terms when weighed against the necessary contributions which came later.

Effective means for biopreservation need to be formulated and implemented. Difficulties arise from land usage pressures and destructive harvesting. Contributory factors include redundancy of overseeing authorities in some regions, inadequate enforcement capabilities and outdated legislation.

RECOMMENDATIONS

1. Suitable compensation for access to biota should be provided as a matter of equity and as a means of promoting improvements in public health and preservation of habitat and species.

2. Contracts for exploration of biomass for the discovery of medicinal agents should make a provision for knowledge provided concerning medicinal properties and uses of the material.

3. National and state jurisdictions should return a reasonable amount of the proceeds from the sale of biological materials to the local or regional area of origin. On the other hand, if arrangements are made locally the right of jurisdictions to reasonable taxation is recognized. Nations, in consultation with their local scientific authorities should think through issues relating to who has the real authority to enter into a binding and enforceable agreement. Rather than see a patchwork of conflicting regulations, it would be far preferable if regional associations of governments and international organizations would set sensible policies for member nations to follow to the extent possible.

4. Payments for removal of biota should be negotiated in advance of collection with appropriate authority and may or may not involve residual royalty rights. The latter issue should also be settled in advance by negotiation. If the species is/are rare or threatened it is expected that adequate provision will be made for the preservation of the species even to the extent of forbidding collection in extreme cases. Government licences and/or supervision by competent scientific authorities will be associated with this work.

5. Indigenous botanic assistance and collaboration through the university system, national museum, departments of natural resources, etc., should be sought with reasonable joint scientific publication rights clarified in advance as appropriate.

6. Support for herbaria and the like should be encouraged as well as for surveys and development of inventories of existing biodiversity.

7. Realistic sharing of subsequently developed knowledge with the originators of the samples, consistent with the needs to protect potential patent and commercial rights, should be practiced.

8. Scientific training should be supported as part of agreements whenever practicable.

9. If cultivation is a practical option serious consideration should be given to doing as much of this as possible at or near the point of origin.

10. The value of extracts prepared close to the point of origin should be compensated following negotiation in advance.

11. In determining payments for products which are marketed, relative contributions to the final outcome must be realistically considered and should be reflected in the level of royalty payments.

12. The concept of capacity enhancement as a consequence of cooperative programs of biota screening for economically valuable constituents is recommended. Aside from its intrinsic merits this can ultimately mature into the local capacity to address some of the unmet medical needs of developing nations. This applies particularly to devastating diseases that are not present or have no relevant counterparts in developed nations. In these cases, research towards cures is comparatively under financed and the fruits of such studies are difficult to develop in practical terms.

IUPAC puts forward these recommendations only as principles to guide actions and negotiations between the involved parties. Detailed contractual provisions are the province of the involved parties and must be determined accordingly as a reflection of the particular circumstances pertaining to individual cases.

APPENDIX

The text of the Manila Declaration and the Melaka Accord follow:

THE MANILA DECLARATION
concerning
Ethical Utilization of Biological Resources

Developed at the Seventh Asian Symposium on Medicinal Plants, Spices and other Natural Products (ASOMPS VII) which was held in Manila, Philippines, from 2-7 February 1992 and was attended by 283 scientists from 37 countries.

Given that:-
1. the maintenance of biological and cultural diversity is of global concern
2. developing countries are major centers of biological and cultural diversity
3. there is increased interest in biological material with medicinal and/or other economic value
4. indigenous peoples frequently possess knowledge that provides a key to natural products of economic value

Recognizing that:-
5. all national governments have sovereignty over their biological resources
6. current practices of exploitation of biological resources and indigenous knowledge are frequently inequitable, favoring technologically advanced organizations and/or developed countries, to the disadvantage of both conservation and development in the country or region of origin
7. there is need for further investment in training and technology in developing countries and for equitable partnerships with developed countries in order to obtain new products from biological material
8. there has been insufficient acknowledgments of essential role that indigenous knowledge (i.e., intellectual property) plays in identifying important natural products.

Thus, it is recommended that:-
9. national governments, with advice from appropriate professional organizations within the region, develop adequate legislation to exercise control over the collection and export of biological materials
10. as a high priority, governments, international agencies, multinational corporations and academic institutions, through training, laboratory construction and technology transfer, should support the development of human and material resources evaluation of indigenous materials for conservation and for managed development
11. for all collecting, the authorizing agreement(s) should include provision for any subsequent commercial development that may eventually arise
12. internationally recognized professional societies develop a code of ethics that facilitates the formation of equitable partnerships in the development of new products from biological material (see Appendix 1)
13. mandatory royalty or licence agreements be established to ensure fair and equitable distribution of benefits to the region of origin
14. supply agreements should only be made by the appropriate country organization and not with individuals in that country
15. in order to avoid over-exploitation of promising species, the country organization should adopt methods to protect the identity and provenance of its biological material
16. specific regulations be established to ensure that the collection and export of biological material is adequately monitored and controlled in the interests of the country supplying the material. These should include the requirements that:

    16.1 collections are made together with local counterparts appointed by the country organizations involved

    16.2 adequately annotated, preserved voucher specimens of biological material are lodged in appropriate national institutions

16.3 sufficient funds are provided by the external organization to cover the support costs which may be incurred
16.4 if there is a threat of destructive harvesting provision must be made for sustainable harvesting or development of alternative supplies
16.5 the traditional knowledge of local participants contributing to development of new natural products must be recognized as significant intellectual property

APPENDIX 1. CODE OF ETHICS FOR FOREIGN BIOLOGICAL SAMPLE COLLECTORS

The reference document was developed at the Botany 2000 Herbarium Curation workshop held in Perth, Western Australia, 15-19 October 1990. It was modified in April 1992 to cover other biological material.

The foreign biological sample collector should:

1. arrange to work with local scientist(s) and institute(s)
2. respect regulations of the country visited, for example, by entering on a research/collecting visitor visa, not a tourist visa, and by observing regulations for export of biological specimens, quarantine, CITES, etc.
3. obtain official permission for all collections in National Parks or protected areas
4. ascertain whether items used in scientific work and which are difficult to obtain in the country of collection can be contributed
5. when applying for a travel/study grant, include equal travel expenses for local counterpart(s) and an amount to cover the cost of processing museum specimens or other costs of the visit to the host institute
6. leave a complete set of adequately labeled duplicates with the institute before departing the country
7. ensure that types of species described as a result of the research are deposited in the National Museum or Herbarium of the country of origin
8. inform the institute in the country of origin where duplicate specimens are to be deposited
9. not exploit the natural resources of the host country by removing high value biological products through collecting wild specimens, for example plants with potential horticultural, medicinal, cultural or other economic value, without prior permission
10. obtain a list of rare and endangered species of the country visited, and do not collect these species without permission
11. collect no more specimens than is strictly necessary; for live plant specimens, collect cuttings or seeds rather than uprooting whole plants; for marine specimens, wherever possible, collect subsections rather than whole organisms
12. leave copies of photographs/slides for the host institute(s)
13. inform the host institute/appropriate organization of new localities of rare/endangered species found
14. remember to send copies of research reports to collaborator(s) and host institution(s)
15. acknowledge collaborator(s) and host institute(s) in research reports and publications
16. collect identified reference voucher specimens for all biological products to be exported

APPENDIX 2. CONTRACT GUIDELINES

ASOMPS VII recognizes that there is considerable variation in the levels of technical expertise for the development of new natural products in the region. There is also recognition that every effort should be made to reduce dependency by developing countries on technology held by developed countries. However in the sort-term efficient development of new natural products may involve sharing of biological resources and technology between developed countries and the country of origin.

In order to avoid contracts which do not achieve equity in partnerships between developed countries and the country of origin, there are suggested minimum standards which should be used:-

1. the amount of material collected for initial screening should not normally exceed 100-500 grams (dry weight) unless specific permission is obtained
2. payment should include all handling expenses and infrastructure costs
3. where screening of extracts is carried out with the aid of a partner organization in the developed world, a minimum of 60% of any income arising from the supply of extract to commercial organizations should be returned to the appropriate country organization
4. the country organization should receive a minimum of 51% of any royalties arising from external collaboration that results in marketable products. Since a fair royalty would be of the order of 3-5%, the appropriate country organization should receive a minimum royalty of 1.5-2.5%.
5. the country organization should not sign agreements that give indefinite exclusive rights to any external party. Exclusivity should be limited to no more than a two-year period
6. complete evaluation of results of any screening should be reported to the supply country organization within a reasonable specified period
7. if there is a threat of destructive harvesting, costs of sustainable harvesting or development of alternative supplies must be borne by the external organization
8. the contribution of research participants should be recognized through coauthorship on publications
9. initial preparation of extracts and screening should be done in the country of origin and assistance to develop this expertise should be provided wherever practicable

THE MELAKA ACCORD

Resolutions ratified by ASOMPS VIII: Eighth Asian Symposium on Medicinal Plants, Spices and Other Natural Products. 12-16 June 1994, Melaka, Malaysia.

Given that in the time since the Manila Declaration was adopted at ASOMPS VII in February 1992:-

- that the Manila Declaration has been endorsed by the Bukit Tinggi Declaration in October 1992,
- the UNCED developed the Conventions on Biological Diversity in 1992 providing for:-
  - the conservation of biological diversity
  - the sustainable use of its components; and
  - the fair and equitable sharing of the benefits arising out of the utilization of genetic resources
- it has been confirmed that the UN Law of the Sea Convention will come into force in November 1994

and recognizing that:-

- the region represented by ASOMPS participants has a wide range of terrestrial and marine biological diversity
- the region has a significant human resource and skills base to conserve and use its genetic resources
- many biological species are not confined in their occurrence to political boundaries

ASOMPS VIII has considered the benefits to be accrued by adopting consistent regional approaches to:-
legislations, policies and procedures relevant to accessing and conserving biological diversity

- involving the scientists of the different component nations in training, research and development related to the sustainable use of that biological diversity
- ensuring the fair and equitable sharing of the knowledge and financial benefits arising from utilization of a Nation's genetic resources

ASOMPS VIII has therefore adopted the resolutions that:
1. Within 1994 each national group of scientists and technologists transmit to their relevant governments the Manila Declaration, noting that its objectives are consistent with those of the UN Convention on Biodiversity, encourages its incorporation in relevant national strategies on conservation of biodiversity, and request that it be brought to appropriate regional bodies, such as ASEAN, for adoption on a regional basis, as a part of this bioregional approach to conservation of biodiversity, within the overall concept of ecologically sustainable development.

As a matter of urgency all nations should develop workable, straight-forward legislation to control the collection and conservation of the biota under their jurisdiction which will be used for bioprospecting.

2. The scientists of each country represented at ASOMPS VIII, in conjunction with the appropriate government agencies in their countries and with appropriate legal advisors should within six (6) months of this symposium prepare and submit to UNESCO-ROSTSEA a draft version of their countries proposed legislation and guidelines on access to, research on, and use of the biological resources of their countries in order to ensure equitable and sustainable development.

UNESCO shall be requested to organize, within eight (8) months of this symposium a meeting of a working group to:
(a) consider the various draft legislation and guidelines
(b) formulate an agreed set of minimum regulations and guidelines concerning these biological resources which might be applicable to all countries involved

The working group should consist of some 20-25 people with scientific, governmental and legal representation from each of the representative countries involved so that definitive and authoritative proposals can be formulated during the meeting.

UNESCO shall be requested to distribute this agreed set of minimum legislation and guidelines together with the various countries's drafts and relevant comments from the working group, to all countries involved in ASOMPS VIII so that these countries can optimize their own legislation and ensure compatibility with those of other countries in the region.

3. We recommend that journal editors, peer reviewers and professional societies should when reviewing manuscripts, grant applications or conference papers attempt to ensure that host country collaborators receive appropriate recognition for their contribution.

4. We recommend that in countries where permit infrastructure exists, all researchers formally acknowledge permit approval by citation of permit number or equivalent) in manuscripts, technical reports and conference papers, and that copies of such papers be provided annually to the permit authorities. In countries where no such permit legislation exists, the national government shall be encouraged to develop such legislation.

5. Nations within the region support the concept of developing regional screening facilities as the first step in stimulating the formation of bioregional drug discovery and development consortia, and establish a working party to further develop this concept.