

Ciba Foundation Symposium 185



ETHNOBOTANY AND THE SEARCH FOR NEW DRUGS

1994

JOHN WILEY & SONS

Chichester · New York · Brisbane · Toronto · Singapore

ETHNOBOTANY AND THE SEARCH FOR NEW DRUGS

The Ciba Foundation is an international scientific and educational charity (Registered Charity No. 313574). It was established in 1947 by the Swiss chemical and pharmaceutical company of CIBA Limited—now Ciba-Geigy Limited. The Foundation operates independently in London under English trust law.

The Ciba Foundation exists to promote international cooperation in biological, medical and chemical research. It organizes about eight international multidisciplinary symposia each year on topics that seem ready for discussion by a small group of research workers. The papers and discussions are published in the Ciba Foundation symposium series. The Foundation also holds many shorter meetings (not published), organized by the Foundation itself or by outside scientific organizations. The staff always welcome suggestions for future meetings.

The Foundation's house at 41 Portland Place, London W1N 4BN, provides facilities for meetings of all kinds. Its Media Resource Service supplies information to journalists on all scientific and technological topics. The library, open five days a week to any graduate in science or medicine, also provides information on scientific meetings throughout the world and answers general enquiries on biomedical and chemical subjects. Scientists from any part of the world may stay in the house during working visits to London.

Ciba Foundation Symposium 185



ETHNOBOTANY AND THE SEARCH FOR NEW DRUGS

1994

JOHN WILEY & SONS

Chichester · New York · Brisbane · Toronto · Singapore

©Ciba Foundation 1994

Published in 1994 by John Wiley & Sons Ltd
Baffins Lane, Chichester
West Sussex PO19 1UD, England

All rights reserved.

No part of this book may be reproduced by any means,
or transmitted, or translated into a machine language
without the written permission of the publisher.

Other Wiley Editorial Offices

John Wiley & Sons, Inc., 605 Third Avenue,
New York, NY 10158-0012, USA

Jacaranda Wiley Ltd, G.P.O. Box 859, Brisbane,
Queensland 4001, Australia

John Wiley & Sons (Canada) Ltd, 22 Worcester Road,
Rexdale, Ontario M9W 1L1, Canada

John Wiley & Sons (SEA) Pte Ltd, 37 Jalan Pemimpin #05-04,
Block B, Union Industrial Building, Singapore 2057

Suggested series entry for library catalogues:
Ciba Foundation Symposia

Ciba Foundation Symposium 186
x + 280 pages, 17 figures, 24 tables

Library of Congress Cataloging-in-Publication Data

Ethnobotany and the search for new drugs / [G. T. Prance, Derek J.
Chadwick (organizer), and Joan Marsh].

p. cm.—(Ciba Foundation symposium ; 185)

“Symposium on Ethnobotany and the Search for New Drugs, held at
the Hotel Praia Centro, Fortaleza, Brazil, 30 November–2 December
1993.”

Includes bibliographical references and index.

ISBN 0 471 95024 6

1. Materia medica, Vegetable—Congresses. 2. Ethnobotany—
Congresses. 3. Medicinal plants—Congresses. I. Prance, Ghilleen
T., 1937–. II. Chadwick, Derek. III. Marsh, Joan.

IV. Symposium on Ethnobotany and the Search for New Drugs (1993 :
Fortaleza, Brazil) V. Series.

RS164.E84 1994

615'.32—dc20

94-28300

CIP

British Library Cataloguing in Publication Data

A catalogue record for this book is
available from the British Library

ISBN 0 471 95024 6

Phototypeset by Dobbie Typesetting Limited, Tavistock, Devon.
Printed and bound in Great Britain by Biddles Ltd, Guildford.

Contents

Symposium on Ethnobotany and the search for new drugs, held at The Hotel Praia Centro, Fortaleza, Brazil, 30 November–2 December 1993

This symposium is based on a proposal made by Professor Paul Cox

Editors: Derek J. Chadwick (Organizer) and Joan Marsh

- G. T. Prance** Introduction 1
- M. J. Balick** Ethnobotany, drug development and biodiversity conservation—exploring the linkages 4
Discussion 18
- P. A. Cox** The ethnobotanical approach to drug discovery: strengths and limitations 25
Discussion 36
- N. R. Farnsworth** Ethnopharmacology and drug development 42
Discussion 51
- W. H. Lewis and M. P. Elvin-Lewis** Basic, quantitative and experimental research phases of future ethnobotany with reference to the medicinal plants of South America 60
Discussion 72
- E. Elisabetsky and D. A. Posey** Ethnopharmacological search for antiviral compounds: treatment of gastrointestinal disorders by Kayapó medical specialists 77
Discussion 90
- A. A. Craveiro, M. I. L. Machado, J. W. Alencar and F. J. A. Matos** Natural product chemistry in north-eastern Brazil 95
Discussion 102
- R. E. Schultes** Amazonian ethnobotany and the search for new drugs* 106
Discussion 112

*Professor Schultes was unable to attend the symposium; his paper was circulated and discussed in his absence.

- M. M. Iwu** African medicinal plants in the search for new drugs based on ethnobotanical leads 116
Discussion 126
- X. Lozoya** Two decades of Mexican ethnobotany and research on plant-derived drugs 130
Discussion 140
- S. K. Jain** Ethnobotany and research on medicinal plants in India 153
Discussion 164
- P. G. Xiao** Ethnopharmacological investigation of Chinese medicinal plants 169
Discussion 173
- G. M. Cragg, M. R. Boyd, J. H. Cardellina II, D. J. Newman, K. M. Snader and T. G. McCloud** Ethnobotany and drug discovery: the experience of the US National Cancer Institute 178
Discussion 190
- S. R. King and M. S. Tempesta** From shaman to human clinical trials: the role of industry in ethnobotany, conservation and community reciprocity 197
Discussion 206
- J. H. Barton** Ethnobotany and intellectual property rights 214
Discussion 221
- G. J. Martin** Conservation and ethnobotanical exploration 229
Discussion 239
- B. Berlin and E. A. Berlin** Anthropological issues in medical ethnobotany 240
Discussion 259
- G. T. Prance** Conclusions 266
- Index of contributors 269
- Subject index 270

Participants

G. Albers-Schönberg Natural Products Chemistry, Merck Sharp & Dohme Research Laboratories, Rahway, NJ 07065, USA

W. Balée Department of Anthropology, Tulane University, 1021 Audubon Street, New Orleans, LA 70118, USA

M. J. Balick Institute of Economic Botany, The New York Botanical Garden, Bronx, NY 10458-5126, USA

J. H. Barton Law & High Technology Program, Stanford University, Stanford, CA 94305-8610, USA

B. Berlin Department of Anthropology, University of Georgia, Athens, GA 30602-1619, USA

L. Bohlin Department of Pharmacognosy, Biomedical Center, University of Uppsala, Box 579, S-751 23 Uppsala, Sweden

P. A. Cox Department of Botany & Range Science, Brigham Young University, Provo, UT 84602, USA

G. M. Cragg Natural Products Branch, National Cancer Institute, Frederick Cancer Research & Development Center, Fairview Center 206, Frederick, MD 21702-1201, USA

A. A. Craveiro Laboratorio de Produtos Naturais, Universidade Federal do Ceará, Campus do Pici, CP 12200, 60.021-970 Fortaleza, Ceará, Brazil

E. Dagne Department of Chemistry, Addis Ababa University, PO Box 1176, Addis Ababa, Ethiopia

E. Elisabetsky Laboratorio Etnofarmacologia, Instituto de Biociências, Universidade Federal do Rio Grande do Sul, Rua Sarmento Leite 500, 90.050-170 Porto Alegre RS, Brazil

- M. P. Elvin-Lewis** Department of Biology, Washington University, Box 1137, One Brookings Drive, St Louis, MO 63130-4899, USA
- N. R. Farnsworth** Program for Collaborative Research in the Pharmaceutical Sciences (M/C 877), University of Illinois at Chicago, 833 South Wood Street, Chicago, IL 60612, USA
- M. M. Iwu** Phytotherapy Research Laboratory, Department of Pharmacognosy, University of Nigeria, Nsukka, Nigeria
- S. K. Jain** National Botanical Research Institute, Lucknow 226 001, India
- S. R. King** Ethnobotany and Conservation, Shaman Pharmaceuticals Inc., 213 East Grand Avenue, South San Francisco, CA 94080-4812, USA
- R. P. L. Lemos** (*Ciba Foundation Bursar*) Instituto do Meio Ambiente de Alagoas, Av. Major Cicero de Gois Monteiro 2197, Mutange, 57.017-320 Maceió AL, Brazil
- W. H. Lewis** Department of Biology, Washington University, Box 1137, One Brookings Drive, St Louis, MO 63130-4899, USA
- X. Lozoya** Instituto Mexicano del Seguro Social, Centro Medico Nacional XXI, Jefatura de Servicios de Investigación Médica, Ed. Academia Nacional de Medicina 4° piso, Avenida Cuahutemoc 330, Mexico DF-CP 06725, Mexico
- J. D. McChesney** Research Institute of Pharmaceutical Sciences, School of Pharmacy, University of Mississippi, University, MS 38677, USA
- G. J. Martin** The WWF/UNESCO/Kew People and Plants Initiative, Division of Ecological Sciences, Man and the Biosphere Program, UNESCO, 7, Place de Fontenoy, F-75352 Paris, Cedex 07 SP, France
- F. J. A. Matos** Horto de Plantas Medicinais, Laboratorio de Produtos Naturais, Universidade Federal do Ceará, Campus do Pici, CP 12200, 60.021-970 Fortaleza, Ceará, Brazil
- A. B. de Oliveira** Universidade Federal de Minas Gerais, Faculdade de Farmácia, Av. Olegário Maciel 2360—Cidade Jardim, 30.180-112 Belo Horizonte MG, Brazil

H. H. Peter Department of Biotechnology/Microbial Chemistry, PH
2.255, K-681.2.42, Ciba-Geigy AG, CH-4002 Basel, Switzerland

C. Pichansoonthon (*Ciba Foundation Bursar*) Department of
Pharmaceutical Botany and Pharmacognosy, Khon Kaen University, 123
Friendship Highway, Amphoe Muang, Khon Kaen 40002, Thailand

D. Posey Instituto Etnobiologica da Amazonia, Conj Maguary, Ala 3,
Casa 1a, Icoracy-Belém, Para, Brazil

G. T. Prance (*Chairman*) Royal Botanic Gardens, Kew, Richmond TW9
3AB, UK

S. M. Rubin Conservation International, Suite 1000, 1015 18th Street
NW, Washington DC 20036, USA

G. Schwartzmann Servico de Oncologia, Hospital de Clinicas de Porto
Alegre, Rua Ramiro Barcelos 2350/sala 2030, Porto Alegre RS, Brazil

P. G. Xiao Institute of Medicinal Plant Development, Chinese Academy
of Medical Sciences, Haidian District, Dong Beiwang, Beijing 100094,
China

Introduction

Professor G. T. Prance

Royal Botanic Gardens, Kew, Richmond TW9 3AB, UK

Many drugs that are on the market have come to us from folk use and use of plants by indigenous cultures. These drugs are being used in some way in modern medicine, but not necessarily for the same purpose as they were used by the native cultures. Very often, something has been used by local peoples because it is biologically active, but a more appropriate use for it in Western medicine is for something different. Folk medicine has been a pointer towards many of the drugs that we use and it is certainly a very useful indicator of biologically active substances. For ethnobotanists, the recent accelerated work on ethnobotany because of the renewed interest of the pharmaceutical and medical world is most welcome. It has helped the science of ethnobotany, not just medical ethnobotany but ethnobotany in general, to advance. One of the reasons the study of ethnobotany has accelerated is that we are aware that if we don't do some of this work now, it will be too late because of the unfortunate acculturation of tribal peoples around the world.

We also need to bear in mind the vital importance of conservation of culture, as well as biodiversity. To my mind, biodiversity gets too much emphasis compared with cultural conservation. We should be asking ourselves: how can our work in ethnobotany help to maintain cultural identity? Several papers in this symposium point out the importance of cultural identity, the importance of tribal customs and of their religions.

This leads on to the issue of ethics. What have indigenous peoples gained from the use of their knowledge by Western culture? I am afraid the answer to date is very little. What have developing countries gained from the use of their genetic material in medicines? This is a hot issue in Brazil. A report from a Manaus newspaper last week, which was also in a national newspaper, had the headline 'Contraband of Amazonian plants to the exterior'—based on absolutely no facts whatsoever. The report says that the New York Botanical Garden is taking plant material for analysis in the National Institutes of Health cancer programme, when they have deliberately avoided doing any work in Brazil. Because of the danger of misunderstanding here, the Garden is extremely careful not to damage its relationship in Brazil so that it can continue the important biodiversity and taxonomic work being done in this country. We need to appreciate the complexities presented by work in medical ethnobotany.

We are working in an area that can easily be misunderstood. We need to leave this symposium with a good sense of the ethics of our future work.

The other interesting development in ethnobotany and ethnomedicine is that we can achieve so much more today because of the amazing improvements in screening techniques through *in vitro* bioassays. So many analyses of plants in the past have not found the active component because the assays were not sensitive enough. A plant that was tested negative 20 years ago would not necessarily give a negative result today.

A problem that I hope we will discuss is the fact that the product used as a medicine by local peoples is usually not what is tested in the laboratory. Most of the effective brews I have seen and experienced are mixtures of green plants in the field. We tend to collect the individual plants, dry them, take them back and then see what chemicals they contain. Something we really have to get over in our ethnobotanical search for medicine is: how can we analyse what the indigenous peoples are really taking? They take elaborate chemical mixtures; chemical reactions occur within the tea that an indigenous person brews, and that is very different from a single compound isolated from a dried plant.

Another problem is the varied chemistry within individual plant species, depending on the ecology, the soil and the climate. We were working at Kew, for example, on a member of the Labiateae for the essential oil that it contained. We were delighted with the amount of the oil that the plant had shown in the field. This plant grew very well in our greenhouses. A chemist harvested it, thinking there would be a lot more of this product for analysis and found that there was none. The seeds were from the same plant that had given a good yield. We persisted with this and after three years of cultivation, suddenly it started producing the desired product in large quantities, probably owing to a change in some local ecological conditions in the growing area or even in the outside climate that we don't know. We often miss things because of this sort of variation. Plants are very sensitive to local conditions; they don't always produce the same chemicals consistently.

Another interesting area is the different concepts of disease between native peoples and practitioners of Western medicine. We often go into our studies thinking of disease in Western terms. We will produce much better results if we learn to understand the concepts and the spiritual side of the medicine of the people with whom we are working. We should not be afraid to discuss that aspect of it here. I believe that ethnobotany includes the knowledge of local folk cultures, as well as of indigenous tribes. For example, I have learned a great deal from the *caboclo* of Amazonia who have taken up many indigenous beliefs and many plant uses. I hope that in our discussions we will not refer only to indigenous peoples, but include the peasant *campesino*, *caboclo*, *ribereno*, *mestizo*, or whatever they are called in different parts of the world.

As a plant taxonomist, I am very aware of the difficulties of identification of the plants studied. Some failures to repeat experiments are often due to poor

taxonomy. Ensuring that our work is backed up by adequate taxonomy is another important issue that needs to be considered.

Finally, a danger associated with the discovery of a new medicine is that the plant species itself can become threatened by overexploitation. We saw this danger coming when taxol was discovered in the Pacific yew, until it could be synthesized from a precursor in commoner yew species. When I was in Cameroon, I saw the *Prunus africana* being eliminated from the forest, as it has been from the forest of most of Africa, because of the commercial exploitation of the bark for medicine for prostate problems. This could be an ideal product for sustainable harvesting, but people are often too greedy, so the entire bark is taken from the trees and the trees die. Promoting sustainable use of the different plants in which useful products are discovered is vital. Here in Brazil, various species of *Pilocarpus* are now endangered through their overexploitation for pilocarpine for the treatment of glaucoma. Fortunately, I think this will end because the company developing the drug is now setting plantations. Nevertheless, some species of *Pilocarpus* are on the brink of extinction.

These are some issues that I hope will come out in our general discussions and in some of your papers.

Ethnobotany, drug development and biodiversity conservation—exploring the linkages

Michael J. Balick

*Institute of Economic Botany, The New York Botanical Garden,
Bronx, NY 10458, USA*

Abstract. Numerous ethnobotanical studies aimed at identifying new pharmaceutical products have been initiated in recent times. Ethnobotany has once again become a recognized tool in the search for new pharmaceuticals. Initiatives by governmental agencies and the private sector have helped spark this renewal. Many of these projects are interdisciplinary efforts involving scientists from the fields of anthropology, botany, medicine, pharmacology and chemistry. The Belize Ethnobotany Project links pharmaceutical prospecting with the conservation of traditional medical systems and biological resources. It illustrates the concept of the 'ethno-biomedical reserve' and provides an opportunity for pharmaceutical and herbal industries to contribute to the conservation effort. Terra Nova Rainforest Reserve is an ethno-biomedical reserve in Belize that was given legal status in June of 1993. Too often the exploitation of wild harvested resources has led to their severe degradation. There is a need for increased efforts to develop technologies to sustain their extraction.

1994 Ethnobotany and the search for new drugs. Wiley, Chichester (Ciba Foundation Symposium 185) p 4–24

In exploring the link between ethnobotany, drug development and the conservation of biodiversity, I would like to address several relevant topics. This paper will report on work done by the New York Botanical Garden staff in collaboration with the National Cancer Institute (NCI). I would like to broaden the scope of the 'drug development' aspect of this paper to include health care in general, whether delivered via pharmaceutical products, herbal formulations or single plant species. As I shall discuss, the conservation of biodiversity can best be achieved through establishing a linkage with the health-care delivery system in its broadest sense.

Ethnobotany and screening for activity against cancer or the human immunodeficiency virus

I previously reported *in vitro* data received from the NCI, comparing the activity of selected medicinal plants against the human immunodeficiency virus (HIV) with that of plants collected randomly (Balick 1990). These results showed that such activity was greater in the medicinal plants. The plant extracts were subsequently dereplicated at the NCI and retested in the HIV screens. Dereplication involves removal of certain components of the crude plant extract such as tannins and polysaccharides. After dereplication, the percentage of plants showing anti-HIV activity falls dramatically and the overall percentage is virtually identical using either random or ethno-directed collection methodology (Table 1). Thus, as Gordon Cragg and his colleagues at NCI have shown with a much larger data set (Cragg et al 1994, this volume), general ethnobotanical collection does not appear to be advantageous in developing leads for HIV treatment.

The question arises as to whether potentially significant compounds are discarded in the dereplication process. Dereplication removes compounds that are known to have immunostimulatory activity. At least one major research programme (King & Tempesta 1994, this volume) shows that potent antiviral compounds can be isolated from tannins.

Another comment may be relevant to an evaluation of the ethno-directed approach involving anticancer therapies. In the field, many plants are collected and documented as being used against 'cancer', after their identification by a field guide or traditional healer. As Xavier Lozoya has pointed out (personal communication), ethnobotanists are usually limited in their powers of medical observation and often fail to include in their notes comments on the type of cancer for which the plants are used, as well as other vital information, such as method of preparation and dosage. From our work in Belize, we have found that several plants are used to treat 'cancer', including *Acalypha arvensis* and *Phlebodium decumanum*. During my first few months of field work in Belize, I recorded these plants as purported to have 'anticancer' activity. However, working with a naturopathic physician and observing the uses of these plants in patients, we realized that the word 'cancer' amongst healers in Belize and

TABLE 1 Percentage of plants showing activity in an *in vitro* anti-HIV screen

	<i>Collection method</i>	
	<i>Random collections (61 samples)</i>	<i>Ethnobotanical collections (73 samples)</i>
Initial screen	1.6	15
After dereplication	1.6	1.3

elsewhere in Central America is really the local word for 'an ailment characterized by severe, weeping open wounds that are chronic, spreading and difficult to heal' (Arvigo & Balick 1994). In order to establish a linkage between ethno-directed sampling and anticancer activity, one must have an intimate understanding of the disease concepts of the culture whose pharmacopoeia is under examination. For the most part, there are few traditional therapies for cancer as defined in the Western sense. It appears that much of the information that has been gathered previously on Central American plants with purported 'anticancer' activity is confused, unclear or has been biased in some way through the collection process. In order to evaluate the ethno-directed approach rigorously and fairly, we need to integrate botany, pharmacology, medicine and traditional beliefs more closely.

Finally, what would the ethno-directed approach yield if the search for anticancer and anti-HIV agents were focused on screening systems and therapeutic treatments other than those involving cytotoxicity? For example, would the plants collected through the ethno-directed approach show significantly greater immunostimulatory activity than those collected randomly? Given present financial and technological limitations, this question may not be answered for many years.

The link between medicinal plants, drug development and conservation

It is usually assumed that the discovery of a new plant-derived drug will ultimately be of value to conservation efforts, especially in rain forest regions. This idea is based on the profit potential and economic impact, as well as the feeling that governments and people will somehow place a greater value on a resource if it or its derivatives can produce a product with a multinational market. The economic value and the potential of medicinal plants to support conservation efforts can be viewed from three perspectives: regional traditional medicine, the international herbal industry and the international pharmaceutical industry (Table 2). The distribution of economic benefits varies greatly. In traditional medical systems, they accrue to professional collectors who sell the plants to traditional healers or to the healers themselves. The local and international herbal industries benefit a broad range of people and institutions, including collectors, wholesalers, brokers and companies that produce and sell herbal formulations. In the international pharmaceutical industry, most of the economic benefit goes to those at the upper end of the economic stratum, at the corporate level, as well as to those involved in wholesale and retail sales.

It is estimated that the international herbal industry is about 10 times the size of the US herbal industry, the value of which is about \$1300 million annually (M. Blumenthal, personal communication). Thus, the market value of traditional medical products, which are used by thousands of millions of people around the world, is thousands of millions of dollars each year. Whether or not this

TABLE 2 The economic value of plant medicines and their potential value for conservation

<i>Sector</i>	<i>Distribution of economic benefit</i>	<i>Amount of taxes collected</i>	<i>Pitfalls</i>
International pharmaceutical industry	Upper end of economic system	Substantial	Overharvest Synthesis (if no provision for benefits included) Plantations established outside area of discovery
National and international herbal industry	Full spectrum of economic system	Medium	Overharvest Plantations established outside area of discovery
Regional traditional medicine	Lower end of economic system	Small	Overharvest (sustainability)

In each sector the market value of medicinal plants is thousands of millions of US\$. The conservation potential of plant use in each sector ranges from low to high.

is comparable to the \$80 000–90 000 million of global retail sales of pharmaceutical products has not been calculated, to my knowledge. However, it can be argued that commerce in traditional plant medicines, consisting primarily of local activity such as previously described, constitutes a significant economic force. If it is assumed that 3000 million people use traditional medicines from plants for their primary health care, and each person utilizes \$2.50–\$5.00 worth annually (whether harvested, bartered or purchased), then the annual value of these plants is \$7500–\$15 000 million, which is comparable to that of the two other sectors of the global pharmacopoeia.

An interesting perspective emerges when the tax yields to government are compared. Obviously, in traditional medical systems, taxes are neither assessed nor paid. The international herbal industry is subject to taxes such as those levied at the point of sale and on corporate profits. Governments benefit most from taxes through commerce for therapies produced and sold by the international pharmaceutical industry.

Those who promote the linkage between conservation and the search for new pharmaceutical products often fail to point out that the time from collection of a plant in the forest to sale on the pharmacist's shelves is 8–12 years and that programmes initiated today must be viewed as having long-term benefits, at best. An exception to this are agreements such as that between Merck, Sharp and Dohme and INBio, the National Biodiversity Institute of Costa Rica.

This agreement provides a substantial 'up-front' payment from Merck for infrastructure development at INBio and for the national parks system in Costa Rica. Hopefully, this will be a model for such North/South collaborations in the future. In traditional medicine and the herbal industry, the yields are immediate and the economic impact on the individual, community and region can be significant.

The potential for strengthening conservation efforts ranges from low to high, depending on whether the extraction of the resource can be sustainably managed over the long term or is simply exploited for short-term benefits by collectors and an industry that has little interest in ensuring a reliable supply in the future. Conservation potential is minimal if the end products are derived from synthetic processes or from plantations developed outside the original area of collection. To address this issue, the NCI's Developmental Therapeutics Program seeks to ensure that the primary country of origin of the plant will have the first opportunity to produce the plant, should commercially valuable products arise as a result of their programme (Cragg et al 1994, this volume).

Table 2 also summarizes the pitfalls inherent in each approach, including overharvesting, synthesis with no provision for benefits, issues of land tenure and the establishment of plantations outside the original range of the species. In any attempt to plan for the maximum conservation potential of a discovery, these must be kept in mind.

Harvest itself is not without pitfalls. One of the primary concerns about extraction is sustainability. A case in point is the extraction of a drug used in the treatment of glaucoma, pilocarpine. The source of pilocarpine is several species of trees in the genus *Pilocarpus*, which occur naturally in the north-east of Brazil, *P. pinnatifolius*, *P. microphylla* and *P. jaborandi*. Leaves have been harvested from the trees for many decades, usually under contract from chemical companies. Limited attempts at sustainable management were undertaken in the 1980s but, for the most part, harvest continued in a destructive fashion. Extinction—of the population in many areas—has been the fate of these plants. Finally, over the last few years, cultivated plantations of *Pilocarpus* species have been developed, which will reduce the value of the remaining wild stands, as well as eliminate any incentive there was for conserving them.

Development of a forest-based traditional medicine industry

As discussed above, one of the primary dilemmas in the development of a programme for extraction of non-timber forest products has been the long history of over-collecting of the resources, with a resultant decline in these resources, as well as the export of raw materials for processing to centres and countries far from their origin. Rattan is a classic example of this overexploitation, with people in producing countries who are closest to the resource receiving the smallest percentage of the profits involved in its

manufacture into high quality furniture. In Central America, as elsewhere, locally developed brands of commercialized traditional medicines are now being marketed. I have seen these brands in Costa Rica, Honduras and Belize during my recent travels there. A key difference in these types of endeavours is that the value-added component of the product is added in the country of origin of the raw material. As these product brands develop, and as new brands and products appear owing to the success of the original endeavours, greater demand for ingredients from rain forest species will result. This could contribute to preservation of tropical forest ecosystems, but only *if* people carefully manage the production or extraction of the plant species that are primary ingredients in these unrelated products. In addition, it is expected that small farmers will cultivate some of the native species, for sale to both local herbalists and commercial companies. To address the latter possibility, our work in Belize has included a project with the Belize College of Agriculture, Central Farms, to learn how to propagate and grow over 24 different plants currently utilized in traditional medicine in that country. Hugh O'Brien, Professor of Horticulture at the College has coordinated this effort, which has included the genera *Achras*, *Aristolochia*, *Brosimum*, *Bursera*, *Cedrela*, *Croton*, *Jatropha*, *Myroxylon*, *Neurolaena*, *Piscidia*, *Psidium*, *Senna*, *Simarouba*, *Smilax*, *Stachytarpheta* and *Swietenia*.

The Belize ethnobotany project

This project was initiated in 1988, as a collaborative endeavour between the Ix Chel Tropical Research Foundation, a Belizean non-governmental organization, and the Institute of Economic Botany of The New York Botanical Garden. The principal purpose of the project has been to conduct an inventory of the ethnobotanical diversity of Belize, a country with significant tracts of intact forest as well as nine different cultural and ethnic groups present within its borders. The project has carried out dozens of expeditions to various locales and has collected some 2700 plant specimens, over 50% of which have ethnobotanical descriptions. The specimens have been deposited at the Belize College of Agriculture and Forestry Department Herbaria, as well as in The New York Botanical Garden and US National Herbarium. A database has been set up at The New York Botanical Garden with planned distribution to several computer facilities within Belize. The project has benefited from traditional knowledge graciously provided by over two dozen traditional healers, of Mopan, Yucatec and Kekchi Maya, Ladino, Garifuna, Creole, East Indian and Mennonite descent.

The ethnobotanical inventory has been combined with a herbarium and literature-based production of a list of the flowering plants and ferns of Belize, with annotations on their common names and uses. This list, which has been produced using the input of over 100 taxonomic specialists, will help provide an idea of the comprehensiveness of the ethnobotanical survey.

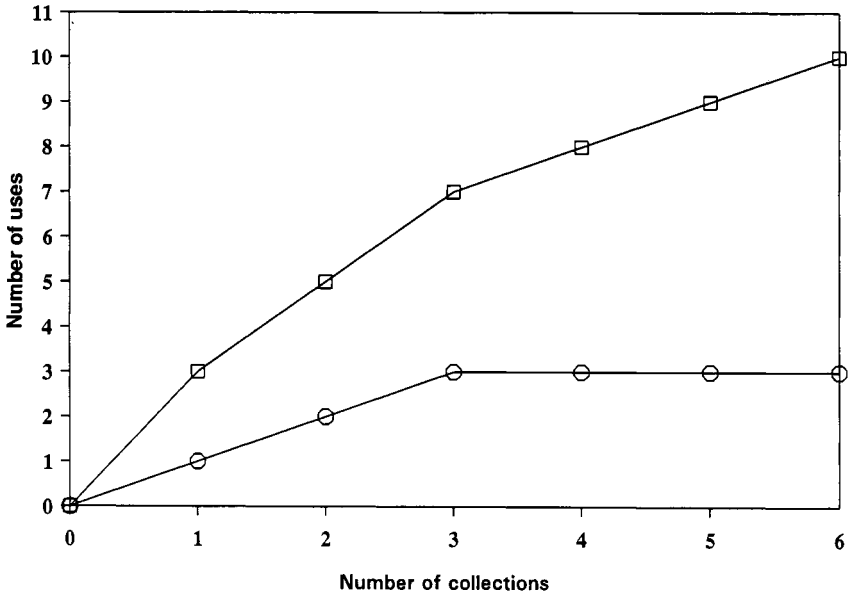


FIG. 1. Multiple use curves for *Vitex gaumeri* (○) and *Neurolaena lobata* (□).

The concept of the multiple use curve

In ethnobotany, a key issue is sample size. When carrying out an ethnobotanical study of a particular group, it is important to determine the number of collections that must be made and the number of people to be contacted before one has a reasonable certainty that the information on a specific plant is relatively complete. Many ethnobotanical studies depend on one or several collections as the basis for their information and conclusions. The adequacy of such numbers of collections or interviews can be assessed using a mathematical relationship based on the concept of the species-area curve (Campbell et al 1986). The resulting 'multiple use curve' shows the relationship between the number of different uses of a particular species and the number of healers interviewed and voucher collections obtained.

Figure 1 shows that for *Vitex gaumeri* the curve reaches asymptote at three different uses. *Yax nik*, as this species is commonly called, is an important medicinal plant utilized for the treatment of leishmaniasis, as well as other skin sores. *Neurolaena lobata* is used as an analgesic, an antimalarial agent and a parasiticide, also to treat nausea, swelling, fever and other conditions. This plant, with its multiple uses, conforms to the concept of a 'powerful plant' discussed elsewhere (Balick 1990). Each individual healer has general uses for the plant, as well as employing it for a specialized purpose. A comparison of the two curves illustrates the difficulty of drawing a general conclusion about the number of

specimens that must be collected before a 'complete' idea of a plant's value can be obtained. In the first, the available information is probably attained after three healers have been interviewed, while in the second, asymptote is not reached after interviews with six healers (Fig. 1). Obviously, the conclusions to be obtained from these data are limited by the small sample size. The six individuals we worked with during the specific collections documented in Fig. 1 are all well-known traditional healers or bush-masters in Belize. The curve would look somewhat different if a country-wide survey of traditional healers were made or an entire community was interviewed for its 'generalist' knowledge. But, it seems fair to conclude that for certain classes of plants, such as medicinals, multiple collections and/or interviews must be made to obtain a complete picture of the knowledge pertaining to an individual taxon. Perhaps with other classes of plants, such as those used as construction materials, the curves would reach asymptote after one or two collections. Application of such multiple use curves to ethnobotanical data sets could add a new dimension to both the planning and the analysis of a particular study.

Figure 2 illustrates the multiple use curve in two different formats. The solid line sorts the data such that each subsequent interview identifies the maximum number of new uses, which is compatible with the protocol for developing a species-area curve. The dotted line represents a chronological presentation of

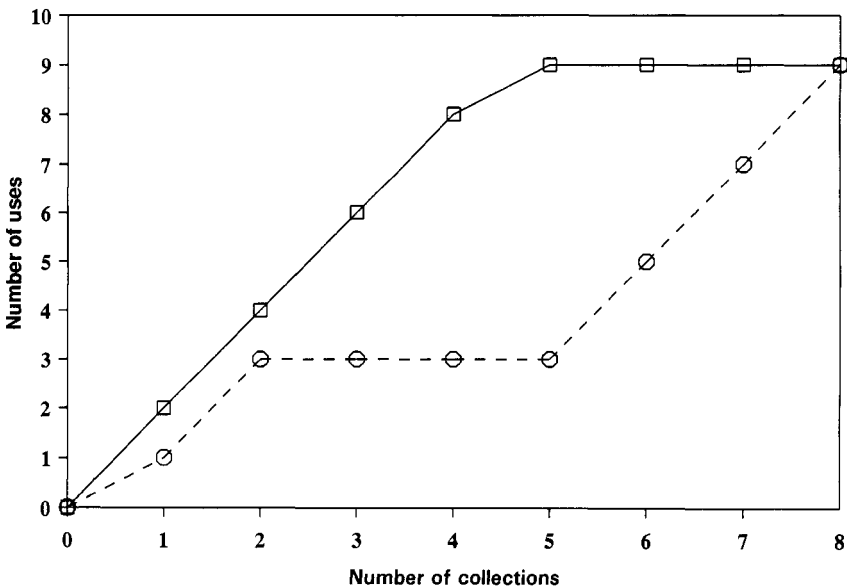


FIG. 2. Multiple use curve for *Piper jaquemontianum* in 'best case' (□) and 'chronological' (○) format.

the data, revealing that if the interview ceased after five collections, it would appear that asymptote was reached at that point. However, healers six, seven and eight all added new information to the curve. Thus, depending on how it is presented, the information in a multiple use curve could be misinterpreted. In this way, the philosophy of the multiple use curve differs somewhat from that of the species–area curve. To avoid confusion, I suggest that the chronological approach be utilized. In addition, the small sample size of ethnobotanical data makes their presentation quite different from the thousands of data points that are common in ecological plots and further supports the use of the chronological approach. The most productive application of the multiple use curve seems to be when relatively large amounts of information (multiple collections) are available for a few interesting taxa.

Valuation studies

One method of ascertaining the value of non-timber forest products in the tropical forest is to make an inventory within a clearly defined area and estimate the economic value of the species found there. Peters et al (1989) were the first to point out the commercial value of non-timber forest products found within a hectare of forest in the Peruvian Amazon. They included medicinal plants in their inventory and, at the suggestion of the authors, this aspect was evaluated in Belize. From two separate plots, of 30- and 50-year-old forest, respectively, total biomasses of 308.6 and 1433.6 kg (dry weight) of medicines whose value could be judged in local markets were collected (Tables 3 and 4). Local herbal pharmacists and healers purchased and processed medicinal plants from herb-gatherers and small farmers for an average price of US\$2.80 per kg. Multiplying the quantity of medicine found per hectare by this price suggests that harvesting the medicinal plants from a hectare would yield the collector between \$864 and \$4014 gross revenue. Subtracting the costs required to harvest, process and ship the plants, the net revenue from clearing a hectare was calculated to be \$564 and \$3054 for the two plots. Details of the study can be found in Balick & Mendelsohn (1992).

Not enough information is available to understand the life cycles and regeneration time needed for each species, therefore we cannot comment on the frequency and extent of collection involved in sustainable harvesting. However, taking the current age of the forest in each plot as the rotation time, we estimated the present value of harvesting plants sustainably using the standard Faustman formula:

$$V = \frac{R}{(1 - e^{-rt})}$$

where R is the net revenue from a single harvest, r is the real interest rate and t is the length of the rotation in years. For a 30-year rotation in plot 1, this

TABLE 3 Medicinal plants harvested from a 30-year-old valley forest plot in Cayo, Belize

<i>Common name</i>	<i>Scientific name</i>	<i>Use^a</i>
<i>Bejuco verde</i>	<i>Agonandra racemosa</i> (DC.) Standl.	Sedative, laxative, analgesic; to treat 'gastritis'
<i>Calawalla</i>	<i>Phlebodium decumanum</i> (Willd.) J. Smith	To treat ulcers, pain, 'gastritis', chronic indigestion, high blood pressure, 'cancer'
China root	<i>Smilax lanceolata</i> L.	As a blood tonic; to treat fatigue, 'anaemia', acid stomach, rheumatism and skin conditions
<i>Cocomecca</i>	<i>Dioscorea</i> sp.	To treat urinary tract ailments, bladder infection, stoppage of urine, kidney sluggishness and malfunction; to loosen mucus in coughs and colds; as a febrifuge and blood tonic
<i>Contribo</i>	<i>Aristolochia trilobata</i> L.	To treat influenza, colds, constipation, fevers, stomach ache, indigestion, 'gastritis' and parasites

^aUses listed are based on disease concepts recognized in Belize, primarily of Maya origin, that may or may not have equivalent states in Western medicine. For example, kidney sluggishness is not a condition commonly recognized by Western-trained physicians, but is a common complaint among people in this region.

TABLE 4 Medicinal plants harvested from a 50-year-old ridge forest plot in Cayo, Belize

<i>Common name</i>	<i>Scientific name</i>	<i>Use^a</i>
<i>Negrilo</i>	<i>Simaruba glauca</i> DC.	To treat dysentery & diarrhoea, dysmenorrhoea, skin conditions; as a stomach and bowel tonic
<i>Gumbolimbo</i>	<i>Bursera simaruba</i> (L.) Sarg.	As an antipruritic and diuretic; to treat stomach cramps and kidney infections
China root	<i>Smilax lanceolata</i> L.	As a blood tonic; to treat fatigue, 'anaemia', acid stomach, rheumatism and skin conditions
<i>Cocomecca</i>	<i>Dioscorea</i> sp.	To treat urinary tract ailments, bladder infections, stoppage of urine, kidney sluggishness and malfunction; to loosen mucus in coughs and colds; as a febrifuge and blood tonic

^aSee Table 3.

gives the present value of medicine as \$726 per hectare. For plot 2, with a 50-year rotation, the estimated value is \$3327 per hectare. These calculations assume a 5% interest rate.

These estimates of the value of using tropical forests for the harvest of medicinal plants compared favourably with alternative land uses in the region, such as *milpa* (corn, bean and squash cultivation) in Guatemalan rain forest, which yielded \$288 per hectare. We also identified commercial products such as allspice, copal, chicle and construction materials in the plots which could be harvested and added to the total value. Thus, this study suggested that protection of at least some areas of rain forest as extractive reserves for medicinal plants appears to be economically justified. It seems that a periodic harvest strategy is a realistic and sustainable method of utilizing the forest. From our evaluation of forest similar to the second, 50-year-old forest plot analysed, it would appear that one could harvest and clear one hectare per year of a 50 ha plot indefinitely, assuming that all of the species found in each plot would regenerate at similar rates. More than likely, however, some species, such as *Bursera simaruba*, would become more dominant in the ecosystem while others, such as *Dioscorea*, could become rare.

The analysis used in this study is based on current market values. The estimates of the worth of the forest could change according to local market forces. For example, if knowledge about tropical herbal medicines became even more widespread and their collection increased, prices for specific medicines would fall. Similarly, if more consumers became aware of the potential of some of these medicines or if the cost of commercially produced pharmaceuticals became too great, demand for herbal medicines could increase, substantially driving up prices. Finally, destruction of the tropical forest habitats of many of these important plants would increase their scarcity, driving up local prices. This scenario has already been observed in Belize with some species. It seems that the value of tropical forest for the harvest of non-timber forest products will increase relative to other land uses over time, as these forests become more scarce.

Establishment of an ethno-biomedical forest reserve

The concept of the extractive reserve as a tool for conservation has received a great deal of attention over the last few years. Many of these reserves involve tracts of forest where non-timber forest products can be harvested by local individuals or groups who then, it is argued, have a stake in the preservation of the biological integrity of the ecosystem. Products such as rubber, Brazil nuts, copal resin, plant oils, fruits, fibre, construction materials, foliage and house plants for the florist trade, and a wealth of other items have been selected for harvest and marketing from extractive reserves in the Amazon, Central America, Asia and Africa. Numerous perspectives on these resources, both positive and negative, have been highlighted recently (Browder 1992, Ryan 1991).

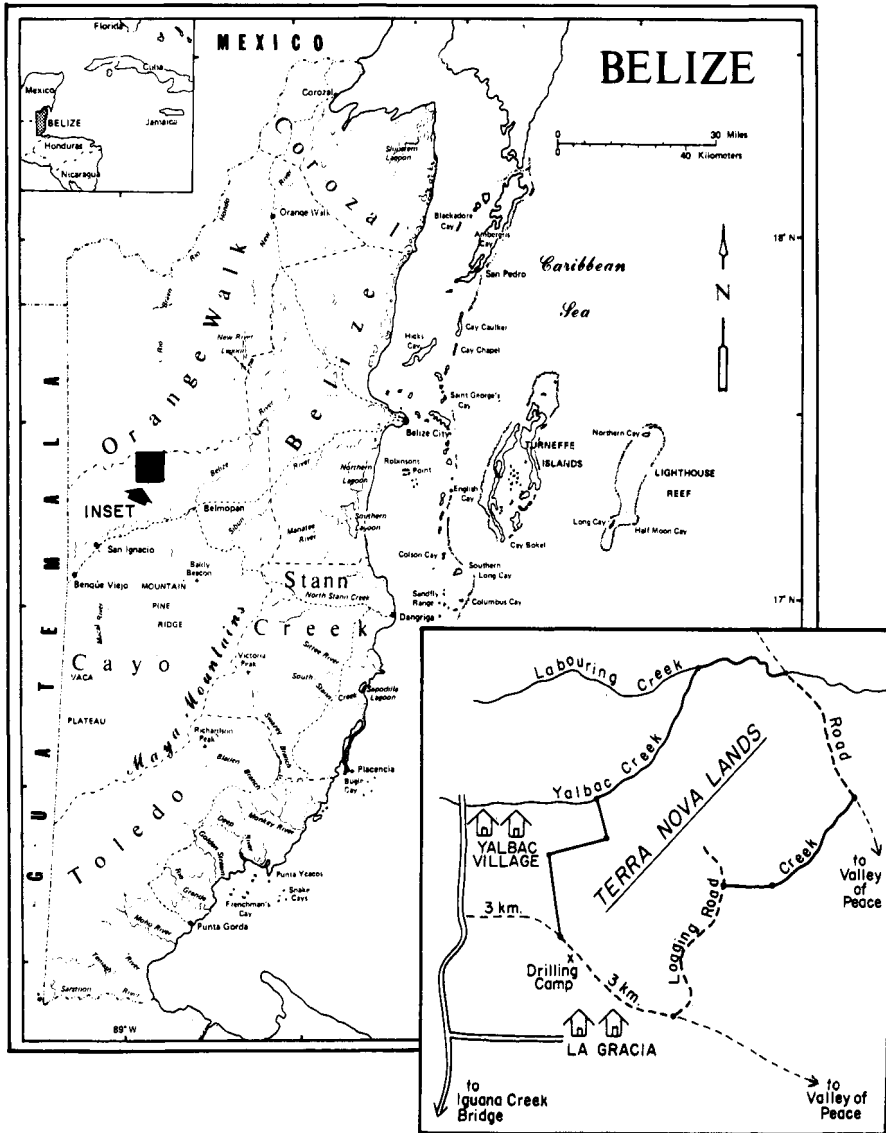


FIG. 3. Map of Belize showing location of Terra Nova Rain Forest Reserve, with inset providing details of the 2429 ha property.

In June 1993, a 2429 ha parcel of lowland tropical forest was given 'forest reserve' status by the government of Belize, to serve as a location for the extraction of medicinal plants, as well as for teaching and apprenticeship. This particular forest, in the Yalbak region of Belize (Fig. 3), contains diverse medicinal plant species. Also within its borders are many different animals, including jaguar, tapir, peccary, howler monkeys, other mammals, birds and reptiles.

The area has been named 'Terra Nova Rain Forest Reserve'. The Belize Association of Traditional Healers has submitted a management plan to operate the reserve. Terra Nova is proposed to have three primary components contributing to its programme and upkeep. Foremost would be the activities of the traditional healers, their apprentices and local students. Trails would be cut, useful plants identified and labelled, and the regulated harvest of materials undertaken. Seedlings of medicinal plants 'rescued' from nearby areas that have been deforested are being transplanted to Terra Nova, primarily by local students, to enrich certain parts of the reserve where the native flora has been degraded. A major concern will be to prevent the overharvest of its economically important components during the initial burst of enthusiasm for the raw materials.

The second component of the proposed programme for the reserve will be ethnobotanical and ecological research, designed to identify the plant resources it contains and develop appropriate technologies for their sustainable extraction. Dr David Campbell from Grinnell College (Iowa, USA) and his students have constructed ecological transects in selected parts of the reserve to serve as long-term study sites. Some of these plots are areas where extraction would take place; in others, changes in the native vegetation would be monitored. Ethnobotanical inventories have been started to catalogue economically important plants in the reserve, as well as in the surrounding Cayo District. Other scientists would be invited to participate in these studies and in archaeological work on some of the sites within Terra Nova.

A third component of Terra Nova's proposed programme is ecological tourism. Belize is host to hundreds of thousands of such tourists annually, who visit its forests, archaeological sites and coastal areas. When facilities and infrastructure are developed, interested visitors would be invited to Terra Nova to enjoy nature walks and to participate in seminars and classes with traditional healers in a forest setting.

A unique feature of this reserve is its focus on the extraction of medicinal plants used locally as part of the primary health-care network. We propose to call this type of extractive reserve an 'ethno-biomedical forest reserve', a term intended to convey a sense of the interaction among people, plants and animals and the health-care system in the region.

It will be many years before this first ethno-biomedical forest reserve can be judged as a success or failure. A great deal of work must go into developing

the management plan and finding the financial and human resources to implement it. Land-use pressures surrounding the reserve, specifically logging and agriculture, as well as sociological and political factors could endanger the long-term existence of the reserve. However, in Belize there is a great deal of optimism about this reserve, in view of its innovative nature, and much support for it amongst the people.

Conclusion

What is the potential contribution of ethnobotany to pharmaceutical development and medicine? As a labour-intensive, long-term endeavour involving highly trained botanists, the most valuable contribution is probably in programmes that are small and tightly focused. High-throughput screening systems in large companies and government laboratories require vast numbers of extracts each month. Given the paucity of knowledge about the chemical composition and full medicinal potential of 99.5% of the plant kingdom, the chance of success of these operations makes it worth using the random approach. The ethno-directed approach is most likely to succeed when it is focused on disease systems actually treated by healers with specific plants. Examples of this might include plants used to treat hepatitis, diabetes, diarrhoea, gastrointestinal problems, skin infections, fungi, wounds, etc. This concept is being tested by the private sector and the results over the next decade will enable a proper evaluation of the ethno-directed approach.

The contributions of medicine to ethnobotany, for the most part, have yet to be realized. In the same way that contemporary ethnobotanists recognize that knowledge of the language and culture of the people one is working with are prerequisites for a full understanding of the uses of plants, we also must combine medical and ethnobotanical skills to obtain a proper understanding of plant use in terms of both Western science and traditional beliefs. This will involve either an interdisciplinary approach with larger teams that include botanists and medical personnel, or an expanded academic curriculum to train those interested in specializing in the medical aspects of ethnobotany.

Finally, I would like to conclude by noting that biodiversity and cultural conservation should be two of the most important objectives of the contemporary ethnobotanist; establishing alliances with those involved in the search for new drugs seems to be an important vehicle for helping to achieve these goals.

Acknowledgements

I am grateful for the collaboration and support of many agencies in Belize, including the Belize Center for Environmental Studies, Belize Zoo and Conservation Center, Belize Association of Traditional Healers, Belize Forestry Department, Belize College of

Agriculture, Ix Chel Tropical Research Foundation and the US Agency for International Development. I should like to thank my colleagues Rosita Arvigo, David Campbell, Sarah Laird, Rob Mendelsohn, Scott Mori, Lon Nicolait, Hugh O'Brien, Polo Romero, Jennie W. Sheldon, Gregory Shropshire and Jay Walker. This paper reports, in part, on research supported by the following sources: US Agency for International Development, US National Cancer Institute, Metropolitan Life Insurance Foundation, The Healing Forest Conservancy, The Overbrook Foundation, The Nathan Cummings Foundation, The Rex Foundation, The Noble Foundation and The Philecology Trust, as well as private gifts.

References

- Arvigo R, Balick M J 1993 Rainforest remedies: 100 healing herbs of Belize. Lotus Press, Wilmot, WI
- Balick MJ 1990 Ethnobotany and the identification of therapeutic agents from the rainforest. In: Bioactive compounds from plants. Wiley, Chichester (Ciba Found Symp 154) p 22–39
- Balick M, Mendelsohn R 1992 Assessing the economic value of traditional medicines from tropical rain forests. *Conserv Biol* 6:128–130
- Browder JO 1992 Social and economic constraints on the development of market-oriented extractive reserves in Amazon rain forests. *Adv Econ Bot* 9:33–41
- Campbell DG, Daly DC, Prance GT, Maciel UN 1986 Quantitative ecological inventory on terra firme and várzea tropical forest on the Rio Xingu, Brazilian Amazon. *Brittonia* 38:369–393
- Cragg GM, Boyd MR, Cardellina JH II, Newman DJ, Snader KM, McCloud TG 1994 Ethnobotany and drug discovery: the experience of the US National Cancer Institute. In: Ethnobotany and the search for new drugs. Wiley, Chichester (Ciba Found Symp 185) p 178–196
- King SR, Tempesta MS 1994 From shaman to human clinical trials: the role of industry in ethnobotany, conservation and community reciprocity. In: Ethnobotany and the search for new drugs. Wiley, Chichester (Ciba Found Symp 185) p 197–213
- Peters CP, Gentry AH, Mendelsohn RO 1989 Valuation of an Amazonian rainforest. *Nature* 339:655–656
- Ryan JC 1991 Goods from the woods. *Forest Trees People* 14:23–40

DISCUSSION

Dagne: Could you make clear to us the difference between a botanist and an ethnobotanist? Is it possible to consider some of the traditional healers as ethnobotanists?

Balick: Many of us are trained in systematic botany in a paradigm that was developed over the last 30–40 years. The paradigm has changed in the last 10–15 years. Contemporary ethnobotany is much more interdisciplinary, integrating ideas from many disciplines with different perspectives. There still needs to be a person who identifies the plants, so that one knows what one is working with.