Chapter 2
Bioprospecting for Pharmaceuticals: An Overview and Vision for Future Access and Benefit Sharing

Danielle Cicka and Cassandra Quave

2.1 Introduction

Before the advent of synthetic chemistry, plants were well known as a primary source of medicine. Still today, medicinal plants are used for healing around the world; in some regions, up to 80% of the population relies on plants as primary sources of medicine (WHO 2002). Conservative estimates show that at least 28,187 plant species are currently recorded as being of medicinal use (RBGK 2017). Though drug discovery has tended toward synthetic compounds, almost half of the drugs approved since 1994 are based on natural products (Harvey 2008). These medicines include some of the world's most essential medicines including acetylsalicylic acid, dihydroartemisinin, pilocarpine, and warfarin (WHO 2017). With the increase of microbial resistance, chronic disease, and heavy burden of communicable disease, new medications are in high demand. Plants can help meet this demand by their unparalleled array of untapped complex chemical diversity.

This chapter gives an overview of the role of bioprospecting in the drug discovery process, the unique regulatory environment for such drugs, challenges in bioprospecting, and a vision for navigating these processes for future discovery.

2.2 Plants in Drug Discovery

Plants play several critical roles in the development of pharmaceuticals. Their unique chemical compounds may be developed into novel drugs as well as become the basis for novel drug classes. Further, the accessibility of plants throughout

D. Cicka · C. Quave (✉)
Emory University, Atlanta, GA, USA
e-mail: cassandra.leah.quave@emory.edu

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history has allowed for much investigation by local communities and this knowledge can be used to assist targeted drug development.

2.2.1 The Story of Paclitaxel

The discovery of bioactive compounds from natural products has had important contributions in several aspects of drug development. The story of the discovery of the natural product paclitaxel, a widely used cancer chemotherapy, exemplifies the contribution of natural product research throughout the drug discovery process.

In 1962, the National Cancer Institute and the United States Department of Agriculture conducted a collection of plants for screening. Through this untargeted mass screening of plant extracts for bioactivity, 4% of extracts were found to have anticancer activity (Suffness and Douros 1982). The Pacific yew (*Taxus brevifolia* Nutt., Taxaceae) was found to have cytotoxic effects. The compound paclitaxel was eventually isolated from the Pacific yew via bioassay-guided fractionation and underwent clinical trials for ovarian cancer (McGuire et al. 1989) and breast cancer (Holmes et al. 1991). Paclitaxel stabilizes microtubules, preventing their disassembly during cell division and is used especially for ovarian tumors, representing a novel mechanism of action at the time (BMS 2011; Schiff et al. 1979).

However, *T. brevifolia* yields a small quantity of paclitaxel, just 0.02% from the bark (Wani et al. 1971). Further, stripping the bark for collection of paclitaxel is detrimental to the survival of the tree and therefore is not a sustainable resource for anticancer treatment. The structure of paclitaxel is so complex that the process of total synthesis is neither time nor cost efficient. To preserve the species, structure-activity relationship (SAR) studies were undertaken to determine the active structural components of paclitaxel necessary for the preservation of therapeutic effect. A related species, English yew (*Taxus baccata* L., Taxaceae) was screened for its microtubule effects (Guenard et al. 1993). A compound in the species, baccatin, was found to be a precursor of paclitaxel, but did not exhibit the anticancer properties. The difference between baccatin and paclitaxel resides in a specific side chain, which was then deemed essential for paclitaxel's bioactivity. Baccatin as well as 10-deacetylbaccatin III is found in higher quantities than paclitaxel in *T. baccata*; 10-deacetylbaccatin III can then be synthesized into paclitaxel (Fig. 2.1). These compounds are found in high quantities in the needles of the tree, providing a renewable resource (van Rozendaal et al. 2000). Paclitaxel can also be more sustainably synthesized from plant cell cultures (Malik et al. 2011) or from fungal endophytes (Stierle et al. 1993). These options allow the sustainable production of paclitaxel in higher quantities.

Paclitaxel is just one example of a lifesaving, natural product pharmaceutical. The structural complexity and diversity of natural products derived over years of selective pressure of plant defenses can not only offer novel treatments, but also add to the repertoire of chemical structures from which drugs can be modeled.

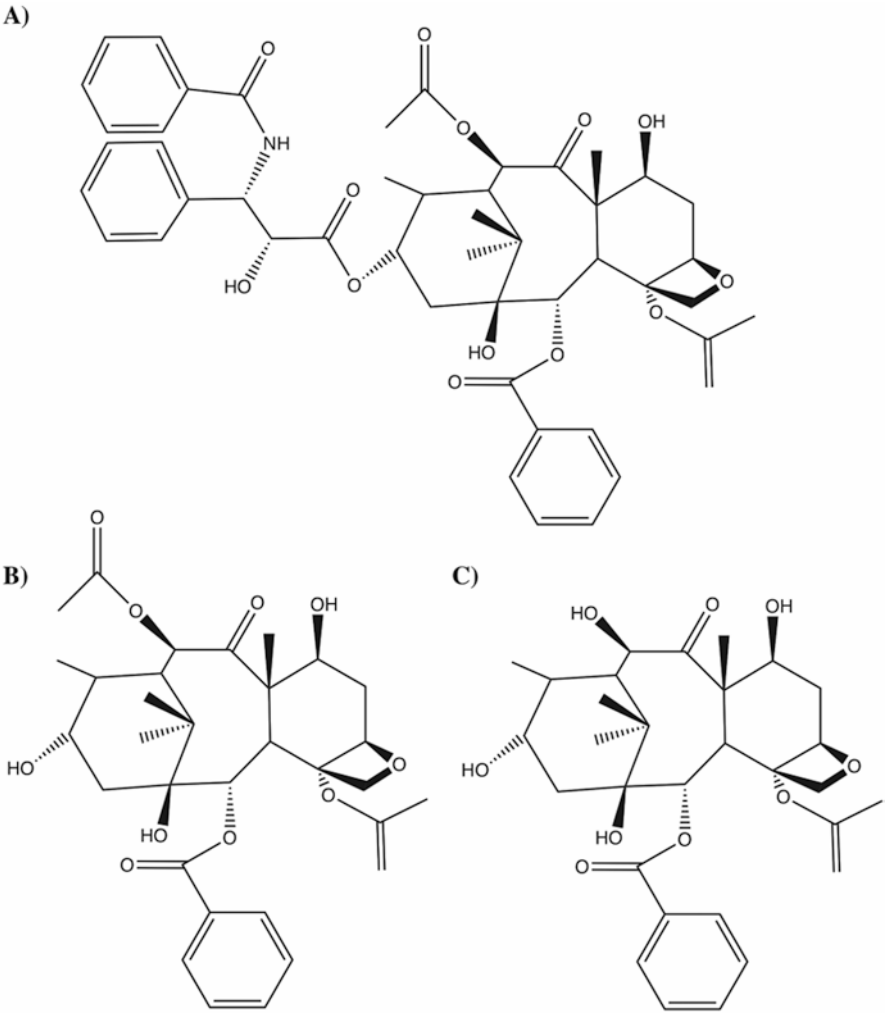

Fig. 2.1 Structure of paclitaxel and its precursors. (**a**) Paclitaxel. (**b**) Baccatin III. (**c**) Deacetylbaccatin III

2.2.2 Structure-Activity Relationship Studies

Bioactive compounds from plants can be used as scaffolds for structure-activity relationship (SAR) studies. These analyses identify the active groups of the compound to determine how modifications can maximize the effect of the compound. As discussed previously, SAR studies were crucial for the discovery of a sustainable source of Taxol.

As natural compounds have greater complexity and diversity than synthesized libraries, the potential for novel structures is great (Camp et al. 2012). There has

been continued use in recent years of SAR studies of natural products in search for treatments for diseases such as malaria, breast cancer, and Alzheimer's (Aratikatla et al. 2017; Lee et al. 2017; Robles et al. 2017). The more natural product structures that are elucidated, the more SAR studies can be completed by comparing the activity of various molecules. Screening large natural product libraries has many challenges compared to synthetic compounds; however, natural products likely already have bioactivity for the plant, and thus may have a high likelihood to be active in other biological systems (Atanasov et al. 2015; Hunter 2008).

2.2.3 Ethnobotanical Approach to Drug Discovery

An ethnobotanical approach to drug discovery is one in which the traditional uses of a plant are taken into consideration when looking for potential therapies in nature. In fact, natural products are more likely to be bioactive when based on ethnomedical data rather than random screens (Elvin-Lewis 2011). Though random screens such as the National Cancer Institute's search for anticancer compounds had viable yields, a more strategic approach can increase prospects of finding bioactive compounds.

The discovery of artemisinin particularly exemplifies this strategy and its necessity for effective drug discovery. Dr. Youyou Tu is credited with the discovery of artemisinin from sweet wormwood (*Artemisia annua* L., Asteraceae). This compound and its derivatives have been widely used as an antimalarial drug, rendering Dr. Tu a winner of the 2015 Nobel Prize in Physiology or Medicine. Artemisia was screened for antimalarial properties in the 1960s as part of a study of traditional Chinese medicine (TCM), but was found to have fluctuating effects on the parasitic infection. However, when an extraction method was developed that incorporated its traditional preparation, the active compound was isolated (DeNicola et al. 2011). Artemisinin-based combination therapies are now recommended for treatment of *Plasmodium falciparum* infections worldwide (WHO 2016).

2.3 Framework for Managing Intellectual Property

Given the successes of bioprospecting, it is essential to preserve natural biodiversity and the capacity of corporations and local communities to continue to develop the potential of natural resources. Care must be taken to ensure the protection of knowledge and maintenance of ethical standards to avoid exploitation of natural products and traditional knowledge while recognizing the financial incentive for companies and local communities to develop lucrative pharmaceuticals. Though this section is not all encompassing, discussion of the regulatory environment is necessary to paint a picture of the hurdles and protections involved in bioprospecting. Even though a

framework exists for navigating the regulatory environment, there is a lack of clarity for its implementation. It is a problem for all parties involved when intellectual property is not protected. This is especially clear when natural products and their indications for use are traditionally used by local communities.

2.3.1 Protecting Intellectual Property of Researchers: Patenting of Natural Products

The process of drug discovery is long and arduous; however, as stated at the start of this chapter, patience is rewarded as there have been many invaluable medicinal discoveries from natural resources. To market active compounds as pharmaceuticals in the United States, the product must meet standards for approval by the Food and Drug Administration as a pharmaceutical. While drugs are being developed and undergoing clinical trials, protection of the investigators' rights to the compound must be maintained. Investigators may seek to secure patents on the active compound while bringing the use of the natural product to commercialization to the public domain. The FDA also grants market exclusivity separately from patents that may have a different time course than the patent for certain pharmaceuticals (FDA 1999). Without patents, discoveries would become public knowledge much sooner, which may inhibit a discoverer from recouping discovery costs as soon as another party is able to market and sell the compound.

There are specific patenting issues to address when working with natural products. Patent laws differ by country and a product can be patented in multiple countries (Worthen 2004). Focusing on the United States in this chapter, patenting natural products has recently been put into the spotlight. In 2013, the United States Supreme Court ruled against patenting of naturally occurring entities such as genes in *Association for Molecular Pathology* vs. *Myriad Genetics Inc*. Due to this case and others before it, the court issued a memorandum on patent eligibility for natural products (Wong and Chen 2014). This document states that a patentable product must be significantly different from its naturally occurring form (Hirshfeld 2014). Therefore, a biologically active natural product likely will have to be modified if it is to be patentable. This lends to the following possibilities for patentable entities. One could possibly patent the altered product itself, the method of production, or a novel use of the product. If the constituents of the product cannot be fully determined, a product-by-process patent may be considered. This does not include products synthesized from a new process that are identical to a naturally occurring product. For one to patent the method of production, the method cannot simply be common knowledge or a general application of the product. The specific dosage, regime, and disease target must be stated (Hirshfeld 2014; Wong and Chen 2014). Though the barriers to patenting drugs may be stringent, they provide some hope for stability and protection in a competitive market in which investment of time and capital is extraordinary.

2.3.2 Protecting Intellectual Property of Local Communities and Biodiversity

Exploitation of natural resources and their guardians is a concern in the pursuit of lifesaving medications. In 1993, the Convention on Biological Diversity (CBD) established rules regarding the protection of biodiversity. This agreement laid the groundwork for fundamental principles of intellectual property rights to protect both economic incentives and maintain biodiversity. The convention established that prior informed consent must be obtained from informants and mutually agreed terms determined in order to achieve adequate benefit sharing (UN 1992). Around the same time, in 1991, the International Cooperative Biodiversity Groups Program (ICBG) was established and provided for benefit-sharing projects. The CBD was an important step; however, it was criticized for its lack of specific requirements, leaving interpretation to individual countries. Thus, the 1995 Agreement on Trade-Related Aspects of Intellectual Property (TRIPS), for members of the World Trade Organization, attempted to fill some of the gaps left by the CBD, particularly by requiring minimum patent laws of member nations (WTO 1995).

Further, the Nagoya Protocol, implemented in 2014, was developed as a supplement to the CBD. Its aim is to ensure benefit sharing when using genetic resources (CBD 2011). It currently has 93 member parties. Most members of the UN have ratified the Nagoya Protocol, the notable exception being the United States (CBD 2017). The Nagoya Protocol aimed to address specific benefit-sharing goals not explicitly addressed by the CBD including promotion of the role of women as stakeholders of traditional knowledge and necessity of explicit capacity-building agreements with developing countries.

The Nagoya Protocol and the TRIPS agreement, though both aimed at the protection of knowledge, highlight different aspects of the protection. TRIPS does not state the importance of benefit sharing, but rather focuses on the importance of maintaining intellectual property rights, often in the form of patents. The Nagoya Protocol focuses more on access and benefit and places intellectual property rights as one of the possible benefits. Various other legal documents to clarify access and benefit sharing have been developed, though mostly by developing nations (Medaglia and Silva 2007). However, these major legislative pieces highlight the different aspects of post-CBD agreements between researchers and local communities. Implementation of the Nagoya Protocol and CBD may be improved by having an overarching regulatory body to help navigate adherence to the protocol.

2.3.3 Organizational Regulations

Various international professional societies have delineated standards for members' publications which help to accomplish the goals of the international regulations. These standards include obtainment of informed consent and engagement of

communities throughout the process. For example, the Society for Economic Botany adheres to the International Society of Ethnobiology Code of Ethics (ISE 2006), which expects its members to uphold communities' rights as historical protectors of the genetic resources and requires informed consent. The American Society of Pharmacognosy also mandates its members to try to protect communities and obtain prior informed consent (Flamini et al. 2002). Though these statements err on the side of vagueness, this may allow each agreement to be shaped to fit the needs of the project and the parties involved.

2.3.4 Managing Expectations

Ethical standards are critical; however, those standards can only be maintained if both parties agree that the standards have been met. Managing expectations of the outcome of bioprospecting endeavors is vital to this mutual understanding of realistic results. With the hope of a blockbuster drug on the horizon, source countries may have unreasonable expectations about the financial gains of partnering with a drug discovery team. Expectations on both sides need to be transparently outlined initially. A typical marketable drug costs $2.558 billion to develop (DiMasi et al. 2016) and can take at least 10 years (NCCIH 2015). Local communities and partnering countries need to be aware that there is no guarantee that a blockbuster drug will be discovered from the partnership. On the other hand, researchers face expectations for publication and revenue generation from their employers. Provisions for conservation and benefit sharing at the initiation of the project can protect against pressure-causing parties to default on vague promises or act on unfounded fears.

Disparities in expectations can arise from differences in the information to which each party has access. Countries supplying natural products may not know how much the products are worth and overestimate their value. They also may not be able to follow the product throughout the research process and therefore enact stringent access regulations. Researchers may distrust their in-country partners since the quality of the natural products may not be transparent and they may not know how their benefits are being utilized (Richerzhagen 2011). Maintaining realistic expectations is difficult but necessary in a field of uncertainty and diversely specialized players.

2.4 Challenges in Bioprospecting

Though there is much promise in bioprospecting for the discovery of novel compounds and uses, there are significant hurdles to overcome in the process. Strides have been made toward improving access and benefit sharing, but the potential ben-

efit of these agreements is still greatly untapped. An interdisciplinary approach may be necessary to harness the potential of these regulatory environments to better serve all parties.

2.4.1 Biopiracy

The fine line between bioprospecting and biopiracy has been a constant debate despite regulations (Rose et al. 2012). The term "biopiracy" is credited to the Rural Advancement Foundation International (RAFI) and generally refers to the use of intellectual property systems to legitimize the exclusive ownership over biological resources and processes that have been historically used in nonindustrialized nations (RAFI 1993).

International cooperative biodiversity groups (ICBGs) were developed in 1991 to be the model for cooperation between drug discovery and protection of knowledge. They supported the ideals of prior informed consent, benefit sharing, local infrastructure development, and biodiversity management (Rosenthal 1997). RAFI's critiques, along with protests from COMPITCH, the State Council of Organizations of Indigenous Traditional Healers and Midwives, against ICBG-Maya caused the project to fold in 2001 (ETC 2001). Critiques also came from the International Society of Ethnobiology for failure to achieve adequate consent and debate ensued over the criteria of such consent. The conflict that arose over ICBG Maya reveals the complexities of remaining an unbiased researcher while navigating a the historical and political landscape as well as managing external pressures and competing voices (Hayden 2003). This case highlights how the very fine line between biopiracy and bioprospecting is subject to interpretation by different participating members.

Biopiracy is still a major concern, though. At a 2002 meeting in Cancun, 17 member nations of Like-Minded Megadiverse Countries made it a priority to ensure the careful protection of Latin America's and South America's unparalleled diversity of plants. Commenting on the status of bioprospecting in this region, Fernando Quezada, Consultant of the Sustainable Development and Human Settlements Division of the Economic Commission for Latin America and the Caribbean, acknowledged that the megadiverse countries have a fear of being taken advantage of and this has resulted in a hindrance to drug development (Quezada 2007).

Stringent legislation regarding bioprospecting stems partly from fear of biopiracy and exploitation of endangered species. This fear is not unfounded for cases such as Brazil where the illegal trade of wildlife is a massively profitable and rampant industry (Rocha 2003). The illegal trade is detrimental to biodiversity and to indigenous communities as protocols for benefit sharing and conservation are not adhered to.

Though the CBD established states' control over access to their genetic resources, these agreements will require careful planning (UN 1992). The Nagoya Protocol combats this problem of biopiracy by providing more specific international require-

ments for research endeavors. Promoting transparency, ensuring accountability, and establishing legal frameworks will need to occur in order for adherence to this protocol (Kursar 2011).

2.4.2 Conservation

The Nagoya Protocol encourages conservation efforts when bioprospecting. Enforcement of these measures is crucial as nonadherence can have devastating effects. For instance, it was found that parts of Bushman's hat (*Hoodia gordonii* (Masson) Sweet ex Decne., Apocynaceae) have dramatic appetite-suppressant effects. The San people, an indigenous group in South Africa, used the plant to suppress appetite while hunting. Phytopharm filed for patents on *H. gordonii* active components; however, this was done without prior informed consent or benefit sharing with the San people. The South African Council for Scientific and Industrial Research intervened to establish an agreement between the two parties (Robinson 2010). Though it is not currently marketed as a pharmaceutical, the publicity generated led to its collection and marketing as a health food supplement by other companies not a part of the agreement (Wynberg et al. 2009). Now, *H. gordonii* is included in Appendix II of the Convention on International Trade and Endangered Species of Wild Fauna and Flora to protect it from unsustainable collection (CITES n.d.). This case highlights the importance of up-front consent and benefit sharing and the importance of ensuring biodiversity within those agreements.

Furthermore, the World Health Organization issued regulations on the collection of medicinal plants for the safety of the species and the users. The regulations prevent overharvesting by prohibiting collection of plants that are scarce and mandating that the source country ensure that the plants do not become endangered. Further, these regulations ensure that plants are identified correctly and are not exposed to large amounts of pesticides or chemicals (WHO 2003). Adherence to the Nagoya Protocol and WHO policies is one step toward the prevention of the detrimental effects of the commercialization of medicinal plants, as seen with the collection of *H. gordonii*.

2.4.3 Sharing of Intellectual Property

There are two intellectual property components at stake—the property of the local communities that provide ethnobotanical knowledge and the property of the researchers that develop the plant extracts into single-compound pharmaceuticals or refined formulations of botanical drugs. Without protected intellectual property, the economic incentive for developing pharmaceuticals could diminish for all parties involved. However, the intellectual property used in the discovery process must be shared respectively among all parties involved in the development of the pharma-

ceutical and contracts must be negotiated fairly and clearly across national and political boundaries. Tangible benefits of sharing intellectual property can take various forms and will be discussed in the future direction portion of this chapter.

There are inherent general challenges when sharing intellectual property. First, determination of who is the rightful owner of the ethnobotanical knowledge can be difficult. Different communities may have similar ethnobotanical knowledge of how to use a plant for medicinal purposes. Determining who should be given benefits and a share in the intellectual property is challenging and is best determined early on in the process of bioprospecting. Researchers have used a variety of definitions to guide them. In ICBG-Peru, it was discussed that all Aguaruna communities would receive long-term benefits and those directly involved with research would receive more immediate benefits. Sometimes, royalties are shared among all communities a company has worked with, a stance taken by Shaman Pharmaceuticals (King 1994; Rosenthal 1997). Naming individuals on patents is a more guaranteed way to ensure that benefits are distributed to locals, but such individual inventors must be defined (USPAT 2015).

2.4.4 Access to Resources

Before the bioprospecting research even begins, there are hurdles to overcome, specifically in obtaining permits to access the plants of interest. Access permits are administered by each individual country. These permits are difficult to obtain in certain countries, to the extent that researchers have been dissuaded from collecting in some regions. For example, Brazil has a multitude of agencies with the power to approve a permit (Silva and Espindola 2011), rendering the permit process unclear and decentralized (Danley 2011). Additional permits may also be needed after access is granted. Permits may be needed to export materials from the country and for additional uses than originally intended (Medaglia and Silva 2007; Silva and Espindola 2011).

2.5 Future Directions in Bioprospecting

The future of bioprospecting will necessitate addressing some of the challenges associated with bioprospecting, especially regarding adequate access and benefit-sharing agreements. To accomplish this, several models of access and benefit sharing have been employed around the world. However, there is no streamlined process for formulating these complex agreements. Ensuring that interdisciplinary players and representatives of all parties are party to forming these agreements can help mitigate some of the difficulties of bioprospecting.

2.5.1 Access and Benefit Sharing

A practical way to ensure protection of intellectual property of host countries is through adequate access and benefit sharing. Though access and benefit sharing have been required by the Nagoya Protocol, there is much room for interpretation. The benefits have taken a variety of forms suited to the project's capabilities and the communities' needs.

Benefit sharing can take two forms: monetary or nonmonetary. For monetary benefit sharing, different payment schedules can be devised, including payments for the plants collected, research using the plants, and royalties from any product developed. Advance payments can also be used, as in the form of trust funds, which can help communities up front during the long drug discovery process (Guerin-McManus et al. 2002; Rosenthal 1997). Patents may provide some monetary benefits, but are generally not considered the best mechanism for benefit sharing with local communities (Greaves 1994) and require that all parties to receive monetary benefit be individually named on the patent for effective distribution of monetary compensation (Rose et al. 2012).

Access and benefit sharing do not solely imply monetary compensation for gains from a blockbuster drug. Monetary compensation may never be a reality as many potential pharmaceuticals fail clinical trials, and many products collected and tested never make it past the laboratory bench. Access and benefit sharing require open communication with the host country and groups throughout the process.

Perhaps equally constructive for local communities are nonmonetary benefits. Maintaining close connections with the host country and the local communities may help mitigate some of uncertainty of loose ties between parties in the lengthy research and development process. These benefits may be in the form of training for the project, capacity building, commitment to research local diseases, or provision for conservation needs. Several ICBGs enacted advance payments for conservation and development projects. In fact, each ICBG had elements of capacity building in the form of community health clinics, herbaria, or equipment for research (Rosenthal 1997).

Collaborations with host country universities can support worldwide research connections. For example, the National Cancer Institute established a partnership with a Panamanian research institute to build local capacity and relations (Rose et al. 2012). Additionally, researchers can assist in the preservation of knowledge by reporting back collected data in a manner that is accessible to the local communities. For instance, books in the local language recording uses of local plants can be gifted to the community. Lastly, there is an untapped market for the pharmaceutical industry to contribute to combating diseases that primarily affect the source countries of their partnerships (Rose et al. 2012). Encouraging pharmaceutical companies to invest in those disease areas could increase the industry's involvement in the neglected disease sector.

Outside organizations such as governmental institutions or NGOs may be necessary to ensure conservation of natural resources long term. Benefits may be given to

the government or NGO as well as in the case of Suriname ICBG and the African ICBG, respectively (Rosenthal 1997). To further ensure adequate benefit sharing, local organizations can empower local communities to become knowledgeable about the contracts they are signing.

Benefit sharing is often undefined, causing remunerations to be forgotten or lost in the discovery process. Because research is often not carried out by the same people for the entirety of the project, original informants or terms of agreement may be ignored (Rose et al. 2012). Further, as stated earlier, determining the recipient of such benefits is important and can take several forms.

2.5.2 The Role of Ethnobotanists

Ethnobotanists provide a crucial link between the protection of indigenous knowledge and the advancement of scientific discoveries due to their close relationship with communities and their knowledge of botany. Ethnobotanists are those generally equipped with botanical and anthropological knowledge, though there are few degree-awarding programs in ethnobotany. While ethnobotanists may seem like the perfect marriage of anthropology and botany, they are still an underutilized source for medicinal plant collections. In a 2010 editorial, the Journal of Ethnopharmacology highlighted the underutilization of interdisciplinary research, though it is a popular buzzword (Heinrich 2001).

Ethnobotanists have the skillset to address the social aspect as well as the botanical aspect of bioprospecting. For example, it is important to address the distribution of botanical knowledge and whether the knowledge differs between lay person and healer in order to correctly choose informants for the project. Knowledge of techniques such as cultural consensus analysis, an anthropological technique to determine the accurate descriptions of local knowledge, can be employed in determining the trustworthiness of information from single informants. Further, a researcher who knows how to correctly collect anthropological data will be better suited to classify illnesses where terminology may differ from Western medicine (Reyes-García 2010).

Botanical knowledge of an ethnobotanist is vital as well since the researcher must have the skills to correctly prepare a botanical voucher and obtain the necessary information on how a plant is prepared for usage (Elvin-Lewis 2011). The ability to integrate anthropological and botanical knowledge will not only provide a robust study of medicinal plants, but also build strong relationships with the community.

Furthermore, registering knowledge in a database may be useful for communities who wish to provide regulated access to their knowledge for data mining of the information collected by researchers (Ningthoujam et al. 2012). Ethnobotanists would be a vital asset in helping to set up such databases in a fashion suited for the community. Countries have already begun to establish databases, but some have expressed concerns about their release until there is a system of international

protection for the information (Elvin-Lewis 2007). The regulation of such databases will be further discussed in the following section.

2.5.3 A Vision for an Interdisciplinary Bioprospecting Strategy

The crux of successful bioprospecting hinges on access and benefit sharing between all parties involved. Partnerships between industrialized and developing nations through bioprospecting have the potential to play a vital role in fostering trust and teamwork. Bioprospectors and local communities both recognize the value in the natural world and can unite around their common respect for nature and its potential to fight illness. Few areas of science incorporate both the traditional and modern views of healing and this can be a major point of dialogue.

These terms of benefit sharing must be clearly delineated before research has begun. While there may not be a standard template for all bioprospecting endeavors, flexibility will allow each project to reach terms that are mutually agreeable to the parties involved. The terms must include provisions for plasticity if needed (Rosenthal 1997). This may necessitate the involvement of an unbiased third party to negotiate the terms. Ethnobotanists could be an important part of that team since they are familiar with the challenges of obtaining knowledge and protecting it.

Public registration of traditional knowledge in databases would allow for large searches for information; however, this would strip the knowledge of some ability to generate revenue. If the knowledge is available to all, it also becomes prior art and cannot be patented according to US law (35 U.S.C. § 102). However, much of the medicinal plant knowledge today is already public. On the other hand, databases with selective access may allow communities to generate revenue from access fees imposed on knowledge for research (Elvin-Lewis 2007). Additionally, knowledge from multiple communities could be registered in a database in which communities only have access to their own information. When there is a question as to whether certain information is unique to a community, software may be used to search the whole database for similar information (Sampath 2005). Elvin-Lewis describes the complexities of establishing databases and defining ownership (Elvin-Lewis 2007).

In an ideal world, a third-party or academic organization would establish an independent organization that could negotiate between local communities, their databases, researchers, and governments (Fig. 2.2). This would ensure adequate benefit sharing, minimizing lawsuits post-discovery. This organization would compile a regulatory board of reviewers for each bioprospecting venture. The board could be based on permanent or long-term representatives from academia representing the areas of anthropology, ethnobotany, law, and basic science. Academics are in a unique position to help subdue biases of supplier countries and researchers, with their general commitment to furthering of scientific knowledge and access to disciplines that work closely with local communities. Others on the board would change for each case, with the minimum following categories being represented: a pharmaceutical company representative, a source country governmental

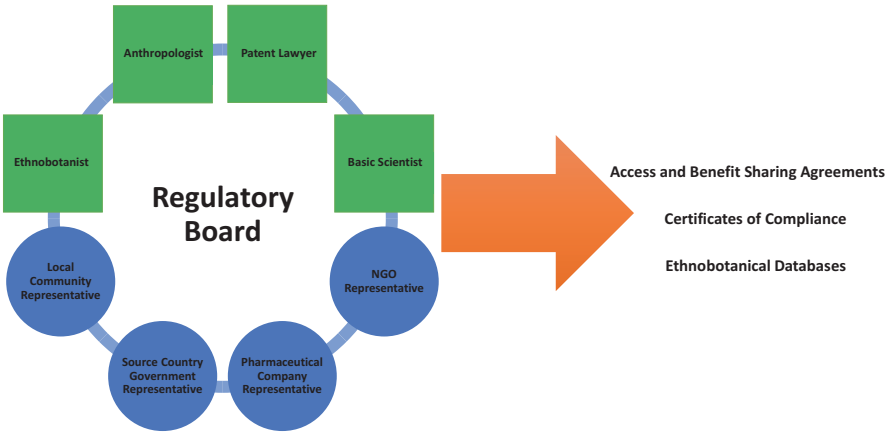

Fig. 2.2 Model for a third-party regulatory board. The board would serve to check the interests and biases of other board members while taking into account each member's expertise. Issues and pressures would be brought to the board to protect the active participants in the agreements. Green squares: long-term members. Blue circles: project-specific members

representative, and a local community representative. NGOs supporting the rights of local communities may be involved as well. The long-term members should be trained in the intricacies of bioprospecting negotiations.

Importantly, this third-party organization could supply certificates of compliance (Richerzhagen 2011) to each party, certifying that each has met the standards of the CBD and Nagoya Protocol. This international indicator of compliance would diminish some of the mistrust and increase transparency in negotiations between parties involved.

Ethnobotanists on the team could assist communities in establishing databases of their traditional knowledge since there is danger of its loss through generations (Benz et al. 2000; Krauss 1992; Ramirez 2007; Reyes-García et al. 2013). They would also be in a position to encourage governments to conserve their biodiversity. When negotiations are made, benefits could be given to the local people and to the governments, to avoid dissemination of benefits through corrupt governmental infrastructure.

The organization could be the mediator between researchers and local databases of knowledge so that local people can effectively capitalize on their knowledge while avoiding pressures from large pharmaceutical companies. It is imperative that local communities and their advocates be vital members of any discussions.

A third party would allow for centralization of negotiations. Many projects have received criticism for failing to interact with communities or provide adequate benefits. Further, researchers have become leery of the difficult legal processes involved in each country. This would take some burden off the researchers and communities and allow centralization of regulatory processes.

2.6 Conclusion

If bioprospecting practices are not established in an easy-to-navigate and enforceable format, they will continue to be circumvented for exploitation of local communities and the environment. Ethical players will be discouraged from entering the bioprospecting business.

Though there is much room for improvement, it is clear that nature's chemistry is complex and rich in diversity and should be utilized to maximize its benefits, especially for those that already use natural products for treatment. This area of scientific endeavor has the opportunity to unite efforts across economic borders if this turbulent area of work can be navigated and result in the centralization of negotiations of individualized agreements that adhere to the ethical and equitable principles of the Convention on Biological Diversity and Nagoya Protocol.

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