

25 years after the 'Rio Convention' – Lessons learned in the context of sustainable development and protecting indigenous and local knowledge

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ABSTRACT

Background: When in 1992 the Convention on Biological Diversity was adopted, it was a response to centuries of exploitative use of biodiversity and to a lack of recognition of the rights of the countries and regions of origin. At the same time, it was an outcome of the increasing drive, especially in many European and American countries, to ascertain more equitable sharing of wealth between the global North and South. It is a result of negotiations between states and driven by political consensus.

Aim: With this review we aim to assess the situation 25 years after the adoption of the CBD, provide an overview on how we got to the current framework and offer a perspective on how such access rights and equitable benefit sharing can be ascertained.

Outcomes and Discussion: Without doubt the CBD has resulted in a new framework for providing and securing access to biodiversity and for equitable benefit sharing. It has since been developed and amended in numerous treaties and protocols, most recently the Nagoya Protocol. This development is both driven by the historical experience of many countries in the exploitative extractions of biodiversity, and indigenous peoples' drive for the recognition of their rights. Examples of exploitative use of biodiversity include the species yielding quinine and rubber. Using *Lepidium meyenii* Walp. as an example, we assess the current patent basis and highlight why in this case equitable benefit sharing proved to be impossible. Today, there are well-established principles in place to establish intellectual property rights, both with respect to a country's ownership of genetic resources, and a research entity's invention based on them. There remains, however, a lack of investment as well as research and development opportunities based on these internationally binding agreements. [In line with the aims of our review, this](#) paper includes an overview on how the current patenting system can be used to ensure that the goals of the CBD can be achieved

Conclusion: In the context of the centuries of exploitative use of biodiversity, 25 years is a short time span and this review reiterates Posey and Dutfields' call (1996) to companies or other outside organization for developing 'a relationship in which the community is an equal partner'.

Keywords: Ethnopharmacology, traditional medicine, Convention on Biological Diversity, Nagoya Protocol, Intellectual Property, *Lepidium meyenii* Walp. (maca)

AIDS	Acquired Immune Deficiency Syndrome
CBD	Convention on Biological Diversity
CSIR	Council for Scientific and Industrial Research of South Africa
EPO	European Patent Office
EZLN	Zapatista Army of National Liberation
HIV	Human Immunodeficiency virus
ICBG	International Collaborative Biodiversity Groups
IGC	InterGovernmental Committee
IP	Intellectual Property
IPER	International Preliminary Examination Report
IPR	Intellectual Property Rights
NIH	National Institutes of Health
NSF	National Science Foundation
PCT	Patent Co-operation Treaty
R&D	Research and Development
RBG Kew	Royal Botanical Gardens, Kew
TK	Traditional Knowledge
USAID	United States Agency for International Development
WIPO	World Intellectual Property Organization

Introduction

The symposium held at the University of Mainz in June 2017 offered an opportunity to take stock of the developments since the landmark Convention on Biological Diversity of 1992 (also well known as the ‘Rio Convention’ or simply the ‘CBD’). Looking back at the quarter of a century since the CBD and looking ahead one must acknowledge that this has been a game changer in the broader context of biodiversity-based research (e.g. Biber-Klemm and Martinez 2016, EU n.d.). Ten years after the CBD’s adoption Le Prestre (2002) argued that the CBD’s success and effectiveness needs to be assessed in terms of ‘learning, capacity-building, network building, transparency and the elaboration and diffusion of new norms’ (p. 269). There can be no doubt that there has been considerable progress in such outcomes. However, indigenous knowledge remains at risk of being exploited without adequate benefit sharing (see Plenderleith 2004) and in the last 25 years the global loss of biodiversity has become a much more urgent global challenge. The ambition has been to ascertain a sustainable development of new products founded on mutually agreed terms of access, and with adequate benefits to the provider countries and local communities.

In the context of medicinal plant research, a key question is linked to the global ability to develop and introduce new medicinal plant-based products. As Le Prestre (2002) points out, the CBD is a ‘deeply wide-ranging, ambitious and political convention’ (p. 270). Also, the CBD has been followed by a series of additional agreements and protocols (most recently the Nagoya Protocol of 2014; <https://www.cbd.int/abs/>) including the Aichi Biodiversity Targets, for the 2011-2020 period (<https://www.cbd.int/sp/targets/>) as well as many complex sets of national legislative endeavours and laws (<https://absch.cbd.int/>). States now ‘have sovereign rights over the genetic resources found within their national jurisdiction.’ Consequently, each state may define the modality of access to natural resources within its boundaries as it relates to research and development. A quarter of a century after the adoption of these basic principles, this may seem obvious, but in this paper we highlight not only how this legislative international framework has come about, but also what legal challenges exist and how these can be overcome. (Heinrich 2013). This is embedded in the wider need to objectively assess using stringent scientific methods the current knowledge on the world’s biodiversity and ecosystems including benefits they provide to people, as well as the tools and methods to protect and sustainably use these vital natural assets (<https://www.ipbes.net>). In 2012 the Intergovernmental Science-Policy Platform on Biodiversity and Ecosystem Services was

established as an independent intergovernmental body (<https://www.ipbes.net>) aiming at achieving this. However, here the focus is less on scientific aspects, but more on the intellectual property resulting from biodiversity and its use.

The long road from exploitation to equitable sharing

Exploitation as a natural ‘right’

A key part of the challenges relating to access and benefit sharing is linked to historical exploitations, where key powers secured access without recognition of local rights, regulations and without benefits to the source countries. Quinine from *Cinchona* species is one of the classical examples (Gramiccia 1988, Heinrich 2013). Before the advent of semi-synthetic derivatives barks of *Cinchona* species and quinine were the prime antimalarial agent. First isolated in 1820 in a pure form by Pierre Joseph Pelletier and Joseph Bienaime Caventou (France); the structure was elucidated in the 1880s by various laboratories. The bark was formerly used as a febrifuge, spasmolytic orexigenic, tonic and astringent. For the colonial powers of the 19th century it was a key resource essential in maintaining the health both of the military and civilians in the colonies. In the 1850’s the British alpaca wool dealer Charles Ledger (1818-1905) exported hundreds of alpacas to Australia without consent. When interest in the antimalarial medicine rose he turned his attention to quinine and specifically to Peruvian or Jesuit’s bark, native to mountainous regions of tropical America. In the bark trade two species are important - *C. pubescens* Vahl (= *C. succirubra* Pavon; red cinchona, ‘cinchona rubra’) and *C. calisaya* Wedd., (syn.: *C. ledgeriana* Moens. et Trim.; yellow cinchona, ‘cinchona flava’). Hybrids and other *Cinchona* species are also used. In 1865 he selected *C. calisaya*, which had a higher yield and without consent brought them to the UK and further on to Dutch and British colonies (as well as Australia). Today it is widely cultivated in South-East Asia and parts of Africa (cf. Gramiccia 1988, Heinrich 2013). Clearly this was detrimental to the countries of origin.

Similarly, *Hevea brasiliensis* (Willd. ex A.Juss.) Müll.Arg. was exported without consent from Brazil by (later Sir) Henry A. Wickham (1846 –1928) for building up rubber plantations in Asia. These seeds were transported via Liverpool and then the RBG Kew with the support of Sir Joseph D. Hooker, one of the greatest botanists). Clearly at the time this was not seen as being the cause of any concern, but without doubt it has deprived the countries of origin and their people of significant benefits (Ponting 2007).

From exploitation to equitable benefit sharing

Many other examples could be cited, but these two highlight the evolving concerns about exploitative bioprospecting and in the decades prior to the CBD, many biodiversity-rich countries pushed for new global arrangements recognising all states as equal partners. These debates intensified in the 1970s and 1980s. in the context of a wider political criticism about the exploitation of the 'Third World'..This includes ones which had only become independent from colonial powers in the decades prior to the CBD and the American Countries, which were approaching the 500th centenary of Christopher Columbus's 'discovery' in 1492. This anniversary provided a focal point for highlighting this exploitative relationship and for arguing for equitable solutions..

Clearly, independent states and their political elite played an important role, but the willingness to develop new models of collaboration were often driven by grass root initiatives and resulted in diverse links and approaches. The most important example in the context of the CBD is the *Declaration of Belem* of 1988 (Posey and Dutfield 1996). Recognition of indigenous rights and a call for increased support for research on ethnobiological inventories on conservation and for management programmes ethnobiologists were at the forefront of developing such novel models of collaboration. One of the main driving forces was the anthropologist and entomologist Darrell E Posey (1947-2001), who also highlighted the rights of indigenous people to such resources (Posey and Dutfield 1996):

'But listening is not enough. We must uphold the basic rights of indigenous and traditional peoples to land, territory, knowledge and traditional resources. And we must discover how the balance sheet of economic and utilitarian policies can be countered by the sacred balance expressed by such peoples.'

These initiatives take it beyond the interests of states, and emphatically argue for the recognition of peoples' rights, most importantly, indigenous cultures.

The CBD as one stepping stone of global agreements.

The CBD is an element in a long list of agreements of states dealing with biodiversity related questions (Table 1). Initially the focus was on the protection of endangered species like the 'Convention on Nature Protection and Wild Life Preservation in the Western Hemisphere' of

1940. All have had a wide-ranging impact on specific fields and have also often been scrutinized, for example, with regards to their (lack of) effectiveness.

The period after the adoption of the CBD has seen many discussions about what constitutes good practice and what is needed to implement it. Key to this have been projects attempting to develop novel medicines from natural resources. However, so far, no example has emerged which could serve as a model on how to develop a commercially viable product on the market which generates revenues to the regions of origin. In the following we limit the discussion to those products which were developed after 1992 and which, therefore, should be based on the principles of the CBD.

Soon after the adoption of the CBD, two US led consortia started research projects with the aim of implementing the principles of the CBD (Heinrich et al 2014). These ICBGs (International Collaborative Biodiversity Groups) received funding through by a combined initiative of the United States Agency for International Development (USAID), the National Science Foundation (NSF), and the National Institutes of Health (NIH). The US government's objective behind the programme was to develop integrative strategies for an "improvement of human health through drug discovery, incentives for conservation of biodiversity, and new models of sustainable economic activity that focus on the equilibrated integration of environmental aspects, human health, population, socio-economic growth and basic democracy" (Rosenthal n.d.). From 1993 until 2003, Dr. Barbara Timmermann and Mexican, Chilean, Argentinian and US collaborators focused on plant species growing in arid areas in Chile, Argentina, and Mexico, in an ICBG-funded project. IP and benefits were to be shared between the partners in an agreed equitable manner and the project did result in a wide range of peer-reviewed articles, conference proceeding and local flora publications as well as capacity building and conservation projects in the host countries. A key concern was the reliability in the supply of plant material in essence bringing the project to a halt (B. Timmerman, pers. Com 27.12.2017)

Similarly, Drs. Brent and Elois Ann Berlin from the University of Georgia (USA) developed an ambitious ICBG (International Collaborative Biodiversity Group) project in Chiapas México (ICBG Maya) with a strong local participation incorporating an intensive dialogue with groups of indigenous people and various Mexican institutions. The focus was to "discover, isolate, and preclinically evaluate pharmacologically important species from Mexico, the third richest mega-diversity region of the world and one of the most threatened in

terms of biodiversity loss due to increased environmental destruction” targeting potential treatments for diarrhoea, respiratory conditions, infectious diseases, contraception, and other locally important health needs. With its base in Chiapas a regions was chosen which in 1994 had seen a popular uprising led by the “*Ejército Zapatista de Liberación Nacional*” [EZLN - Zapatista Army of National Liberation]. Early on conflicts with national and foreign non-governmental organizations arose, which ultimate let to an early end of the project. Both Elois-Ann and Brent being co-signatories of the Declaration of Belem (see above), they had a keen interest in indigenous and local rights, but had no opportunity to implement their access and benefit sharing agreement. The ICBG Maya was criticised very heavily as being exploitative and was never fully implemented. Both examples also demonstrate that at the time very high expectations were put into what the potential benefits could result from exploring the biodiversity of these regions (Heinrich 2013).

Shaman Pharmaceuticals is another important example. Based on Wayne Inman, the idea behind this company’s strategy is simple “We want to utilize this information base that native people have, to recognize that they have had a long history of using these plants” (Wells 1998). Equitable benefit sharing was a key element of the company’s strategy. *Croton lechleri* L. known in Spanish as *sangre de drago* or *sangre de grado* (Schultes and Raffauf 1990) is a great example of natural product-based drug discovery, but in the end not of equitable benefit sharing. Used traditionally in the Amazon to treat diarrhoea it had been document widely for example by Richard E. Schultes in the 1930’s). It was one of the prime product leads of Shaman Pharmaceuticals (1989 – 1999). However, in 1999 the company had to end their pharmaceutical development and in 2005 the efforts ended in bankruptcy. In 2012 Crofelmer (Fulyzaq[®]) was licensed first in the USA for the treatment of secretory diarrhoeas associated with acute infections including cholera, chronic diarrhoea associated with HIV/AIDS, and diarrhoea-predominant irritable bowel syndrome. The extract of *C. lechleri* has a good clinical and pharmacological evidence-base, but no benefits to local communities are known (Heinrich 2013).

Another interesting case is *Euphorbia peplus* L. another Euphorbiaceae. In Europe and Morocco it was widely used to treat warts and other skin conditions. These records date back several centuries, but no detailed review on its medical uses in Europe are available. With the arrival of white settlers and prisoners, the species was introduced into Australia as well as into other regions of the world. The species use to treat skin cancers and solar keratoses was recorded during the 1970s and 1980s in the region of Brisbane. An Australian company

Peplin Ltd., developed peplin (or ingenol 3-angelate) for use in actinic keratoses on the face, scalp, trunk and extremities. In 2009 the company became a part of LEO Pharma, Denmark and in January 2012 a gel with (0.015%, 0.05%) ingenol mebutate was approved by the US Food and Drug Administration (FDA), and soon afterwards in the same year in Brazil, Australia and the EU (as Picato[®]). In addition, R&D for intravesicular treatment of bladder cancer and systemically against leukaemia are ongoing (Heinrich 2013). In the absence of any demands no effort has been made to ascertain benefit sharing and obviously, one must ask, with whom a company could come to an agreement. In addition this example also demonstrates that taxa which have a wide geographic distribution (especially weedy species) and ones which have been introduced outside of their native region of origin pose a particular challenge. Many cultures or human groups and different countries could lay claims to it but as pointed out in this paper, the CBD recognizes a country's sovereign rights to plants that grow in that country.

In addition one could cite a number of plants developed into supplements and functional foods, but again no examples of benefit sharing are known. The most extreme case is likely to be the Hoodia plant [*Hoodia gordonii* (Masson) Sweet ex Decne.] from Southern Africa (see Heinrich 2013). The active compounds were patented in 1997 by the CSIR (Council for Scientific and Industrial Research of South Africa). Importantly the developments in the 1990's were started and while agreements were in place between the CSIR and a small U.K.-based small company (Phytopharm Ltd.) but no benefit sharing agreements were in place until several years later. Hoodia is a traditional food and medicinal plant of the San. However, the patents did not recognize this, nor was this done with their prior informed consent. Understandably, the San, and indigenous ('bushmen') group of the Kalahari Desert and other stakeholders raised concern about this lack of intellectual and financial recognition. Finally, in 2004 the San and the CSIR signed a benefit-sharing agreement, which in fact would become one of the first benefit-sharing agreements. It gave the San a share of royalties derived from the sale of products containing the patented extract. Specifically, the following agreement was reached:

- CSIR will pay the San 8% of all milestone payments it receives from its licensee, U.K.-based Phytopharm plc
- CSIR will pay the San 6% of all royalties that it receives once the medicine is commercially available
- CSIR will make study bursaries and scholarships available to the San community

- CSIR and the San people agree to collaborate in future bioprospecting for the benefit of both parties (see Heinrich 2013).

While in this case an agreement was in place, the developments of hoodia first into a potential medicine (Pfizer) and later into a food supplement (Unilever), were both stopped presumably due to a combination of safety concerns and supply problems (since this is a very slow growing desert species). The failure here does not lie in the intellectual properties and the associated benefits, but ultimately, in an approach, which ignored problems in the context of the product's safety and supply.

The last example – the famous case of artemisinin from *Artemisia annua* L. – predates, in terms of the initiation of R&D efforts, the changes implemented with the CBD and differs in other aspects from the previous ones. It was initiated in China during the cultural revolution and here the benefits in essence lie in the compound's use for treating malaria, and as such its benefits also to many people in Southern China (Tu 2016).

Based on these examples, some key problems emerge which have prevented progress of the projects:

- Problems in securing a reliable access to a region which are based on an equitable partnership. This is often linked to unclear legal arrangements
- Inflated expectations of stakeholders in the region of origin
- Unrealistic scientific-economic expectations

Thus, multinational industry feared that IP in a country's natural resources could reduce the legal certainty needed when investing in research and development, and compromise its own IP. On the other hand, IP rights are often mistrusted by developing countries, where most of the world's biodiversity exists. It is this latter reluctance to embrace IP rights and the principles of the CBD that we wish to explore in this paper.

Overview of IP Protection

Criticisms of the patenting of natural products

The use of intellectual property protection in the field of ethnopharmacology / natural product research has often been the subject of negative comments. Patenting, in particular, has been considered as a mechanism that can be misused to encourage biopiracy. One well known example is the Indian Neem tree (*Azadirachta indica* A.Juss.); a European Patent was granted

relating to the anti-fungal effect of a neem oil formulation. The case drew added publicity because the joint Patentees were the US Corporation W.R. Grace, and the US Government Department of Agriculture. One review of the facts is called “A Briefing Paper on the Neem Biopiracy Case” (Bullard, 2005). The patent was revoked after opposition, based on prior use in Indian agricultural practice. *As Bullard states, it was argued that 'the fungicidal effect of hydrophobic extracts of neem seeds was known and used for centuries on a broad scale in India, both in Ayurvedic medicine to cure dermatological diseases, and in traditional Indian agricultural practice to protect crops from being destroyed by fungal infections.'* In other words, the patent was anticipated by Traditional Knowledge. The Patentees argued that their formulation differed from those used in traditional practice, but the European Patent Office held that the difference was obvious and therefore not inventive.

Even today, the debate continues as to whether the Neem case is a one-off situation, or whether known genetic resources or Traditional Knowledge are frequently being patented. In 2014, Singh et al (2014). stated “Patent is [the] main tool for biopirates” and concluded that:

“Biopiracy is immerging scientific nuisance in pharmaceutical business. It can commercialize locally as well as globally well-known facts, inherited knowledge, traditional knowledge, community wisdom, etc., in order to explore new opportunity and cost saving in pharmaceuticals research and development.”

The value of Intellectual Property

The global debate on Intellectual Property Rights (IPR) is often characterized as a “North - South” issue, i.e. suggesting that there are differences between the interests of developed and developing nations. In fact, in the field of phytomedicine, developing countries can benefit from the patent system, by encouraging use and commercialization of their genetic materials, as envisaged by the CBD.

The development of a commercial product based on natural resources is an increasingly expensive process, particularly in the pharmaceutical industry. For any company to make the considerable expenditure in research and development, it needs to have a period of exclusive marketing to recoup that investment. A strong and effective patent provides that limited period of exclusivity, and is an essential factor to develop a new medicine. The CBD

provides the country of origin not only with a right of ownership of the genetic material, but also with the right to share the benefit of any commercialization. So, the intellectual property rights inherent in the CBD work in conjunction with the global patent system (for more details see Hesketh 2015).

A negative perception of patenting in the natural products field could deter biodiversity -rich countries from taking advantage of the commercial opportunities of which patents are part. The decline in interest of large pharmaceutical companies in natural products as drug leads is at least in part driven by this perception. It is therefore valuable to shed some light on practices in the patenting of natural products, by studying one example. We present a brief analysis of patents filed on the Peruvian plant ‘maca’ (*Lepidium meyenii* Walp.), an example which illustrates that inappropriate use of IP proves to be ineffective, but unfortunately could fuel the negative perception of the patent system.

How the patent system works

First, however, it is useful to summarize the operation of the patent system and the mechanisms in place to grant valid patents (cf. Hesketh 2015).

A patent is a national right. To gain patent protection, an applicant must apply to the IP Office, or Patent Office, in each country in which a patent is desired. Those national authorities have the responsibility to examine patent applications to determine if a patent should be granted on the subject matter of the application. Although each country has its own national patent laws, the main requirements of patentability are generally the same, namely *novelty, non-obviousness (or inventive step), and usefulness*. The process to grant (or refuse) a patent is usually called ‘examination’ or ‘prosecution’; it involves a detailed search of the prior art by the National Patent Office, which then starts a dialogue with the applicant. There are some regional Patent Offices, the main one being the European Patent Office (EPO). The EPO, (which is not a EU body), allows a single patent application to be made in respect of a large number of European countries. It provides a one search and examination process to provide a bundle of individual national patents. Secondly there is a system for filing a single international patent application under the Patent Co-operation Treaty (PCT). It is operated by WIPO (World Intellectual Property Organization). WIPO does not issue patents, but provides an initial search and opinion on the patentability of the subject matter.

All major patent authorities around the world, including the U.S. Patent Office, the EPO and WIPO, have highly effective search capabilities. They make every effort to grant only valid patents; and have the resources to do so.

One important point to bear in mind is that the Patent Offices focus on written documents as prior art. Even without written documents, it is possible to draw the attention of a Patent Office to examples of prior use, or other publicly available information, such as traditional knowledge. This is what happened in the Neem case. However, the level of evidence required to establish prior use is much higher than prior written material. That emphasizes the advantage of recording local and traditional knowledge in writing. It provides a simple mechanism to ensure that such knowledge is not patented.

The Maca Example.

In order to provide a balanced commentary on the issue of IP protection of natural products, we chose to consider the example of maca (*Lepidium meyenii* Walp.), because it is an ancient traditional food and medicine from Peru, and has gained international prominence as a new herbal medical product or supplement (botanical). A review (Beharry and Heinrich, 2018) summarizes the species' traditional uses as a food and medicine and its emergence as a global commercial product, especially for its reproductive health claims. Because of the interest in the properties of maca, it has attracted significant patenting activity; and so is a good candidate to study the question of whether patents do contribute to biopiracy. The species is native to Peru and adjacent countries (Ecuador and Bolivia). The patents discussed here were developed based on material from Peru and in collaboration with researchers from these countries.

The WIPO Intergovernmental Committee (IGC)

Maca is also a suitable candidate for an IP study because it has been the subject of representations by the Government of Peru. One document, in particular is worth noting. The World Intellectual Property Organization (WIPO) operates an 'Intergovernmental Committee on Intellectual Property and Genetic Resources, Traditional Knowledge and Folklore' (The IGC). Established in 2000, the IGC is a forum where country delegations discuss the intellectual property issues that arise in the context of access to genetic resources and benefit-sharing. At the 5th session in July 2003, the delegation from Peru submitted a document

entitled “Patents referring to *Lepidium Mayenii* (maca)” [Delegation of Peru, 2003]. In its introduction, the document states:

“The patents referring to *Lepidium meyenii* or maca are one more example, among many which exist, of how the intellectual property system – by means of patents – is based, mainly in the United States, on the privatization of biological and genetic components...”
and

“... many food-related, nutritional and medicinal uses of maca, claimed in these patents, have traditionally been used by the indigenous peoples of Peru.”

What can be achieved analysing one example?

Global issues surrounding IP rights can be complex, especially when combined with the additional factors of the CBD and rights to a country’s biodiversity. Publicly expressed views can often be taken out of context and lead to further misconceptions. Our contribution to this debate is to take an objective view using one example – the patenting surrounding maca – as a basis to review the allegation that the international patent system is being used to unreasonably monopolize the use of natural plant materials or traditional knowledge. To achieve that, we compile a list of relevant patents (or applications) and consider each one in turn.

Approach for analysing patents from *L. meyenii*: Search strategy

A patent search was carried out through the European Patent Office ESPACENET (<https://worldwide.espacenet.com/>) system, for patent cases containing the words *Lepidium meyenii* in either the title or abstract. That search strategy is not necessarily comprehensive to find any patent that could generically cover the maca species, but our objective here is only to find and review some examples of patents that do relate specifically to that plant material. The ESPACENET search was carried out on 2nd December 2017 and resulted in 263 patent cases.

A similar search via WIPO PATENTSCOPE on the same day, again selecting cases with the words *Lepidium meyenii* in the title or abstract, resulted in 159 hits, reflecting the differing database. Again, as the present exercise was focussed on finding representative samples, rather than a comprehensive search for all relevant patents, there was no need to explore the

different results between the two search engines. Because the ESPACENET search produced a larger number of patents, that list of 263 cases was used as a basis for further analysis. Having obtained a list of results from a specific search strategy, it is important to narrow the list in a rigorous and transparent manner, to demonstrate that selections made are not influenced by either subject matter, or predetermined views on the issue in question. What we provide is a selection based on facts rather than opinion.

Selection of patents for comment

Most of the maca patent cases identified were filed in only one country, predominantly in China. Because maca has been commercialized mainly in China, we wanted to check that the large number of Chinese patents was not atypical of the patenting in the herbal product field. Therefore, a similar search was carried out for açai (*Euterpe oleracea* Mart., Arecaceae), a supplement which since about 2005 has become particularly popular in the USA. A search for patent cases with “açai” in the title or abstract resulted in 127 patent cases. For the açai example also, the largest category of patent filings was represented by single-country filings made in China, demonstrating that the patenting of plant species as herbal remedies is common practice in China, irrespective of where the main commercial market is. The breakdown of filings for maca and açai is shown in Table 2:

Table 2: *Lepidium meyenii* - patents filed in a single country and in multiple countries

Because of the global nature of criticisms of the IP system, our efforts focus on maca patents that have been filed in multiple or major Western countries. Therefore, from the list of 263 maca cases, the single-country patent filings are not part of our objective, unless the single country is a USA, PCT, or (all of) Europe. That leaves 13 cases to be reviewed.

Patent cases

The 13 selected patent cases are identified below, with a commentary on each. All of the patent numbers referred to below, and their corresponding publicly available files, can be accessed online in ESPACENET.

Maca as an optional ingredient

The three patent cases in Table 3 relate to inventions in which maca an optional ingredient. The focus of these patent applications is not maca, so they are not considered further.

Table 3 - *Lepidium meyenii* as an optional ingredient*Combinations of ingredients*

In four cases maca is one of several ingredients in a mixture (Table 4). A combination of multiple ingredients can often provide valuable patent protection, especially if all the ingredients are essential to produce the effect. The potential weakness of such patents, especially if there are more than two ingredients in the mixture, is that they can be avoided by omitting just one ingredient.

It is important to note that no combination patent can prevent or inhibit traditional uses of the single natural product.

The patents, or applications, in Table 4 appear to have inventive merit, based on the documents in the publicly available files. They protect inventions and are not of unduly broad scope. Indeed, many are very narrow in scope. They cannot be characterized as attempts to monopolize a natural product or traditional knowledge.

Table 4: Patents on *Lepidium meyenii* - Combinations with other substances*Patent cases of specific relevance to maca*

The remaining 6 cases have greater relevance to the issue we are considering as they relate more specifically to maca. We comment on each one separately below, labelled A to F. By way of explanation, some of the terms and abbreviations used in these commentaries are as follows:

Written Opinion

The report from the designated WIPO searching authority, providing an opinion on patentability. It is non-binding, but can be taken into account by the national patent offices.

IPER

International Preliminary Examination Report, produced if further examination is requested from WIPO.

Priority date

The date of first filing, anywhere in the world, on which the other international applications are based.

Prior art

Information that is published, anywhere in the world, before the priority date of the patent application.

Patent Case A

Title:	Extract of <i>Lepidium meyenii</i> for pharmaceutical applications		
Priority date:	3 March 1999		
Applicant:	Pure World Botanicals Inc (USA)		
Countries:	Australia	AU 3864900	Abandoned
	Canada	CA 2362858	
	Europe	EP 1180006	Refused
	USA	US 6,267,995;	Limited
	PCT	6,428,824;	Negative written opinion
		6,552,206	
		WO 0051548	
Subject matter:	Compositions that can be isolated from <i>Lepidium</i> plant material, useful for treating and preventing cancer and sexual dysfunction. Preferably from maca.		

This family of patent applications is the subject of the 2003 submission from Peru to the WIPO Committee, referred to earlier. Our independent summary of the facts is as follows:

Within the PCT application, the Examination Report (IPER), produced by the US Patent Office on behalf of WIPO, cited two main documents, Comas (1997) and Dini (1994). Both documents refer to extraction of the maca plant. The IPER document expresses the view that none of the claims of the patent application possessed an inventive step.

The European application was refused, based on the knowledge of maca as a cultivated Andean plant and its use for nutritional and medicinal purposes. The Refusal decision from the European Patent Office (EPO) relies on 10 documents, including Comas (1994) and Dini (1994). It points out that Dini also reports the known use of maca for increasing human fertility. The Applicant argued that the invention was in a new process of water then alcoholic extraction, followed by column chromatography, which enriches non-water-soluble components; it was also argued that the folk uses of maca had not been scientifically proved.

However, the EPO held that no unexpected effects were produced. All claims of the application were refused.

In the USA, the broad claims were also rejected, and very limited patents were granted:

- 6,267,995 (a composition - with very limited formulation claims)
- 6,428,824 (a method of treatment of sexual dysfunction, using the limited composition)
- 6,552,206 (one novel compound: N-benzyl-16(S)-hydroxy-9-oxo-10E,12E,14E-octadecatrieneamide)

Commentary on Case A

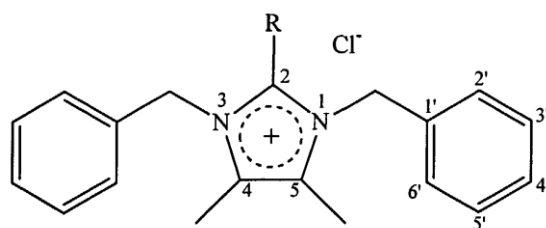
Thus, this series of patent applications did not succeed, because the subject matter was already known. The two citations, Comas (1994) and Dini (1994), show that maca is known to have medical properties. In the U.S., some patents were granted, but limited to very specific formulations.

Overall, this patent series does appear to represent an example of an attempt to obtain patents of undue breadth based on the natural product maca. From that point of view, we agree with the sentiment expressed by the Peru delegation. Nevertheless, no broad patents were obtained. In particular, this case does illustrate the point that mere scientific confirmation of a traditional use does not confer patentability. Isolated compounds can be patented, even though they may have existed in a natural environment. Such a patent would not interfere with use of the plant material itself.

Patent Case B

Title: Imidazole alkaloids from <i>Lepidium meyenii</i>		
Priority date:	14 Aug 2002	
Applicant:	Pure World Botanicals Inc (USA)	
Countries:	Australia	AU 2003265433 Abandoned
	China	CN 1684680 Abandoned
	Europe	EP 1536787 Abandoned
	USA	US 6,878,731 Method of treatment – Granted
		US 2005171081 Compounds – Abandoned
	PCT	WO
		20040162126

Subject matter:



where R = H (compound 1) or methyl (compound 2), as novel compounds, for use against proliferative diseases, such as cancer.

Novel compounds isolated from maca are claimed in this case. As well as the two specific compounds (1 and 2 above) isolated from maca, the patent application claimed a broad scope of derivatives, with multiple substituents at all positions of the rings. Compounds 1 and 2 were the only two compounds exemplified.

In Europe, the EPO found that the broad generic scope of claim was not novel over prior art. Of the two specific compounds, the EPO found that compound 2 was inventive because of its cytotoxic activity, but the activity of compound 1 was only weakly active so was not patentable. Despite the inventive merit of compound 2, the application was specifically abandoned.

In USA, patent 6,878,731 was granted relating to a method of treatment of bladder carcinoma, pancreatic adenocarcinoma, breast carcinoma, or ovarian carcinoma, using compound 1 or compound 2. The compounds themselves were claimed in a related application in the USA, 2005171081. That application was rejected by the US patent office over prior art. The Applicant did not refute the argument, but instead allowed the application to become abandoned.

Commentary on Case B

The issue in this case is not whether the compounds described are found in nature, but instead it is an example of overly broad scope of the definition of the compounds, with insufficient evidence of activity. That issue can arise, and often does, in the patenting of synthetic molecules, just as much as it can with naturally-derived compounds. In this case, the single compound 2, was patentable, but that finding could not be extrapolated to a broad class of compounds claimed.

In most countries, compounds isolated from natural plant materials are generally patentable, provided they fulfil the remaining requirements of novelty and inventive step. The USA has, since 2013, become an exception to that generality, but in other countries, the compounds in

isolated form are considered novel as they do not exist in that form in nature. Such patents are not infringed by the use of the original natural material, so do not affect known or traditional uses thereof. In the particular example of Case B here, the applicant decided not to pursue compound claims, but the hurdles presented by the Patent Offices were not related to the natural origin of the compounds. However, one must also keep in mind that this does not prejudice against a company ascertaining appropriate access right and benefit sharing agreements for these natural resources.

Patent Case C

Title:	Peripheral blood flow-improving composition		
Priority date:	31 Mar 2004		
Applicant:	Suntory		
Countries:	Japan	JP 2005281272	Refused
	USA	US 2008260874 and US	Refused
	PCT	2009269424	Negative opinion -
		WO 2005094860	abandoned
Subject matter:	A composition for improving peripheral blood flow, comprising, as an active ingredient, an extract of a plant of the genus <i>Lepidium</i> , (including maca), for use in a food and beverage product, perfume, cosmetic, or pharmaceutical product.		

This family of patent applications claim a considerably broad scope of uses of extracts of maca. The Japanese application was refused because a peripheral blood flow improvement agent containing an extract of a maca for food and drinks, perfumery and cosmetics, or pharmaceutical products could easily be accomplished based on prior knowledge. No refutation was made.

The WIPO Opinion also referred to the knowledge of maca extracts in foods, drinks, cosmetics and medicines, and viewed the claims as lacking novelty. The PCT application was not progressed internationally, except in the USA.

The US application was refused because the use was inherent over prior knowledge of maca extracts. Again, no refutation was made.

Commentary on Case C

All the patent applications in this series were refused because there was nothing new in the maca compositions covered, or in the uses to which they are put. It was not the natural material itself that was the cited; it was the knowledge of maca products already in use. The blood flow improving property was inherent from the known compositions.

This case presents an example of an attempt to obtain an overly broad patent for maca extracts. A new use may have been patentable, but not if it is suggested by prior knowledge. It demonstrates that inherent ideas will not be accepted as patents.

Patent Case D

Title:	Oral skin moisturizer		
Priority date:	31 Mar 2004		
Applicant:	Suntory Ltd (Japan)		
Countries:	China	CN 1938039	Refused
	Korea	KR	Refused
	Japan	20060135005	Refused
	USA	JP 2005281271	Refused
	PCT	US 2008020067	Negative opinion
		WO 2005094859	
Subject matter:	An oral skin moisturizer comprising, as an active ingredient, an extract of a plant of the genus <i>Lepidium</i> . A preferred active ingredient is maca		

This case relates to an orally ingested composition of maca extracts which significantly improve the moisture-retaining ability of the skin. However, the formulations used are not distinguished from prior oral dosage forms of maca. The references cited against these applications include Cases A and B above. In addition, the PCT Written Opinion also cites a Japanese patent application, JP 2003-238432, which describes the moisture-retention food products containing natural products, one of which is maca.

Commentary on Case D

Here, the alleged invention was the property of maca oral formulations to provide a moisture-retaining effect of the skin. But, once again, all the applications were refused, because

compositions were found to be the same as oral dosage forms previously used. Even the moisture-retaining property was found to have been described earlier.

A new use of a natural material may be patentable, if a formulation can be devised to distinguish from the known uses in some way. Unfortunately, this case did not do that, but it does not necessarily represent an attempt to misappropriate earlier knowledge.

Patent Case E

Title:	A preparation for infertility treatment		
Priority date:	21 Jul 2006		
Applicant:	Angelo Chierigati (Italy)		
Countries:	Italy	ITBO20060544	
	Europe	EP2051724	Refused
	PCT	WO2008012628	No claim found inventive
Subject matter:	A preparation for infertility treatment, comprising: <i>lepidium meyenii</i> ; manganese; vitamin E; selenium; and zinc		

The use of maca in the treatment of infertility was known prior to this application, and is referred to therein. The proposed invention is the addition of the other substances, manganese, vitamin E, selenium and zinc.

The PCT Written Opinion cites a document that discloses that maca preparations inherently contain some manganese, vitamin E, selenium and zinc. The Opinion finds that all of the claims lack inventive step.

In the European case, the EPO relied on the documents cited in the Written Opinion. In addition, third party observations were made by Andres Valladolid of Peru, and by the Government of Peru. The documents cited by those third parties included the 2003 Peru submission to the WIPO committee. In response, the Applicant argued that maca contains only small quantities of manganese and that an increased amount of manganese improves the sperm DNA. However, the EPO held that insufficiently relevant comparative data had been submitted to demonstrate the effect of manganese. The European application was refused.

Third Party Observations can be made to the EPO on any pending patent application, although the person or entity filing such a document does not become party to the proceedings. In this case, the EPO was already aware of the most relevant prior art, but additional views can always be helpful in their deliberations.

Commentary on Case E

In this case, there was an attempt to patent a formulation of maca with added ingredients, but there was not sufficient difference from the level of those materials in maca, either in the natural state, or in known maca products.

This example also represents a scope of patent claim which was shown to be too close to the natural product. It may well be that an additional amount of manganese could provide an improvement over existing maca products and be patentable, but that could not be substantiated by the patent applicant. The result merely fuels the argument of attempts to patent what was already known in nature.

Patent case F

Title:	Dietary supplement for treating erectile dysfunction
Priority date:	2 Sep 2009
Applicant:	Phyt-immun GMBH
Countries:	PCT WO2011026500 Abandoned
Subject matter:	Composition comprising dry extracts of <i>Tribulus terrestris</i> and <i>Lepidium meyenii</i> for the treatment of erectile dysfunction.

This PCT application was abandoned, following a negative Written Opinion from WIPO.

One of the documents cited in the search report, published with the PCT application, is Rowland (2003). The Written Opinion states that the document “is a review of plant derived and herbal approaches to the treatment of sexual dysfunctions which includes phytochemicals such as maca andina (*Lepidium meyanii*) and *Tribulus terrestris*.”

Commentary on Case F

This company attempts to patent a combination of maca with another species, for treating erectile dysfunction, when both species were known to possess that activity.

At first sight, therefore, this may appear to be a failed attempt to patent the known properties of natural products. That is not necessarily the situation however. The PCT specification in question, 2011/026500, does acknowledge the known properties of the species, but alleges that the mixture of the two improves production of testosterone in a synergistic manner. However no supporting evidence of synergy is provided, either in the specification, or later during dialogue with patent offices. This example does illustrate the point that, although synergistic mixtures of known substances can be patentable, evidence is needed to demonstrate that fact.

Implications of the analysis

Our short review paints a picture of some aggressive patent filings relating to maca. The six patent applications that we located were all found to be excessively broad and too close to the natural product to be patentable. All were either refused by the patent authorities, or abandoned. Some of the outcomes may be explained by misunderstandings of patent requirements, but some clearly are not. We do not suggest any deliberate attempt to patent either what is known in nature, or traditional knowledge. The overly broad applications are more likely to have arisen from a poor knowledge of the prior art. A more realistic scope of claim, or more relevant data could have resulted in valid patents.

Nevertheless, a superficial reading of the facts can create a perception of developed countries trying to capture the biodiversity of developing nations. In fact, that is hardly a tenable conclusion. Patenting is an expensive process. Expenditure is only warranted as an investment to obtain a patent that can provide meaningful protection. There is no value in obtaining invalid patents.

The maca analysis demonstrates that: (a) companies and individuals do try to push the boundaries of what can be patented, but (b) the international patent system does not grant patents for subject matter that does not meet strict patentability requirements, so refutes the suggestion that known genetic resources or traditional knowledge is ‘privatized’.

The real issue here is not the patenting of natural products, but the lack of engagement with the countries of origin of the materials from the initial idea to the final stages of product development. Interestingly, one of the more positive conclusions of the Peru 2003 WIPO IGC submission is:

“As the country of origin, Peru should consider the possibility of participating much more actively in the research and development processes relating to plants and biological materials...”

The CBD, especially via implementation of the Nagoya Protocol, provides the apparatus for inclusion and should greatly assist countries of origin to fully participate in the process to develop commercial products from their biodiversity and benefit from strong and effective IP protection.

A successful model would be based on an open dialogue and co-operation between biodiversity-rich countries and commercial partners. On the one hand, those conducting R&D

and seeking to commercialize natural resources must respect the ownership rights of countries and indigenous communities. Access agreements, informed consent and benefit sharing agreements need to be in place at an early stage and an assessment of sustainable supply must have resulted in the supply being feasible. A project plan of research, patent, and commercialization activities should be created in collaboration between the parties, will full communication at all stages (Fig. 1). Instead of filing patents which appear to misappropriate traditional knowledge, a partnership with the county of origin would inform the direction and progress of the research to result in a strong patent of value to both sides.

On the other hand, developing countries need to appreciate the value of intellectual property resulting from carrying out research on their biodiversity / genetic resources. Instead of criticizing the patent system, they could be part of it and appreciate the benefit that could accrue from strong IP which adds value to genetic materials.

The critique of benefit sharing continues, the cases discussed here highlight both how – even if there is the good will to ascertain best practice, major challenges remain, but also that the existing legal mechanisms can be useful to safeguard the rights of the providers and contribute to the search for new medicines and supplements. First, the CBD provides IP in the form of *ownership rights* to genetic resources. Secondly, IP in the form of *patents* can maximize the chances of commercial success and increase the benefit returning to the country of origin. The examples discussed throughout this paper highlight that the problems have not been the protection of the IP, but the lack of a development strategy, which is sustainable and is based on a dialogue between the parties and their informed consent. Patent protection is essential, for example, in the field of new medicines. Without a patent, there would be no possibility for a commercial outlet for the genetic resource, because no pharmaceutical company would invest the huge sums needed to develop a commercial product without a period of exclusivity on the market, to be able to recover those costs. Although not every product will succeed, those that do will be high value products marketed globally. A share of those global sales will be returned to the country of origin (by virtue of the CBD rights). Thus, the higher the sales - protected by a patent - the greater the benefit to the country.

Following the above principles, successful and equitable access and benefit sharing can be achieved by the steps summarized in Fig 1.

Fig 1. Proposed Access and Benefit-Sharing Model: Steps to an equitable and sustainable route to achieve successful, yet equitable, access and benefit sharing and product development

General conclusions

The analysis of historic and modern practice must draw one to the conclusion, that the development of new products must from the start be based on dialogue between the countries of origin and the people who are the original keepers of knowledge and those planning to use it. We reiterate Posey and Dutfields' call (1996) to companies or other outside organization for developing 'a relationship in which the community is an equal partner'. Shaman Pharmaceuticals attempted this with great enthusiasm and the model is still a valid approach today, albeit with more careful attention being paid to the long term nature and costs of such research and development efforts. We also acknowledge that this puts particularly strains, for example, on academic institutions, and appropriate simple mechanism must be in place for research, where the development of novel IP is a possibility, albeit one which is unlikely and also a secondary outcome of a project (with the main outcome being for example the training of junior researchers from the countries of origin). In these cases, other outcomes are much more essential compared to commercial goals. Modern natural product-based drug development (and of other high value products) in fact will have new opportunities if it is based right from the start on an assessment of a sustainable supply, ascertaining mutually agreeable terms for the right to access and developing novel products. While examples for this are available, 25 years post-Rio this still remains a challenge for all parties.

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Both authors have engaged with biodiversity-related projects for many years. Some of the arguments in this publication were further developed based on previous publications (including Heinrich 2013 and Hesketh 2015).

Conflict of Interest

The project received no external funding. AH is CEO of Indigena Biodiversity Ltd. and provides expert advice on intellectual property related aspects of biodiversity and its use.

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Tables and Figure headings

Table 1: The long road to new forms of engagement relating to the use of biodiversity: Some key events relating to the development of international biodiversity-related and access and benefit sharing agreement

Table 2: *Lepidium meyenii* patents filed in a single county and in multiple countries ([all patents are available through ESPACENET - https://worldwide.espacenet.com/](https://worldwide.espacenet.com/))

Table 3: *Lepidium meyenii* as an optional ingredient (see <https://worldwide.espacenet.com/>)

Table 3: Patents on *Lepidium meyenii* - Combinations with other substances (see <https://worldwide.espacenet.com/>)