Bioprospecting in Australia - Sound Biopractice or Biopiracy?

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This contribution investigates the search for new medicines from the vast 'library' of natural products. It touches upon the issues of Indigenous knowledge; intellectual property rights; access to resources; biotechnology and copyright/patent law; and the impact of these factors on research for drug discovery and development. The notorious case of 'Smokebush' and the anti-HIV active compound conocurvone provides a vehicle to promote discussion of these issues and their possible resolution.

Bioprospecting and the search for new drugs: Quest for the golden fleece?

Resistance to antibiotics, the lack of cancer treatments and the threat of novel diseases, such as HIV/AIDS, have fired the search for new drugs. These are frequently derived from natural substances (mostly plant materials) that provide templates (or lead molecules) that theoretical chemists modify and that organic chemists synthesise. Pharmacologists evaluate the biological activities of these products before multidisciplinary teams trial the resulting drugs in clinical settings and get approval to market their collective discoveries. It is a multi-billion dollar industry. There is a constant push to discover and develop new drug entities, and to market them to a public wanting cures.

Accordingly, new drug leads are required to fulfil market needs. Where do these come from? Who foots the bills? Who gets the credit? Who gets paid? And importantly ... who misses out?

The dependence of bioprospecting on biodiversity: Let's not kill the goose that lays the golden eggs

Bioprospecting depends on the existence of considerable biodiversity, "the variability among living organisms and the ecological complexes of which they are part" (Novartis 2005), to maintain a large 'library' of organic molecules to supply the medicines of the future. The natural realm surrounding us is a panoply of variation and hence diversity. There are literally millions of organic compounds elaborated by a conservatively estimated 250,000 so-called higher plant species (Pietra 2002). Of these, it is estimated that about 170,000 grow in tropical rain forest areas with about half of these exclusive to the Americas (Pietra 2002).

Australia is considered one of the 12 'megadiverse' countries, which together account for around 70% of the world's species. In particular, it is estimated that there are between 6,000 to 8,000 species of vascular plants in the 'south-west corner' (Shark Bay to Esperance) of Western Australia, with perhaps 3,000 species as yet undiscovered (Government of Western Australia 2007).

Conservation actions and programs are a priority because there is significant biodiversity unique to Australia and limited knowledge of our species (Boden 1995). Threats of extinction to native species include factors such as unsustainable agricultural practices, introduced species and changed fire regimes. Governments periodically publish extensive reports detailing changes to the environment and measures recommended to help preserve the biodiversity (e.g. Government of Western Australia 2007).

Drugs from the Amazonian jungles: stealing from the poor to give to the rich

The activities of ethnobotanists were popularised through the works of Mark Plotkin (1993, 2000) which recount his travels in the Amazonian rain forest, and his encounters with the native medical practitioners (or shamans). Before Plotkin, there were other North American scientists, such as Richard Evans Schultes. They trekked through forests collecting plant samples with a view to subjecting them to extraction, biological activity studies and phytochemical analysis, for the purpose of discovering and developing new medicines (especially antibiotics) to combat the decreasing efficacy of the armamentarium of drugs available to Western medicine and its practitioners.

It was 'open slather' in the early days of bioprospecting – there were no rules. The north (of America) required drugs and the south (of America) was the source of

lead molecules. There was little concern for the welfare and the traditions of those living 'south of the border' or the equator. It was a 'one-way exchange' where the archetypal ethnobotanist visited a remote tribe in Central or South America, interviewed the medicine man and went off on an expedition into the jungle to collect plants to send back home for analysis (Johnston 1998).

> We of the more 'enlightened times' no longer plunder the intellectual property of Indigenous people. Rather, we (are meant to) seek a fair exchange of knowledge and revenue. All parties benefit ... and it is a sustainable enterprise to boot! This is the hallmark of the 'new ethnobotany' (Johnston 1998).

Drugs from the West Australian Bush: Smokebush Piracy?

Richard W Spjut was a distinguished ethnobotanist employed by the U.S. National Cancer Institute (NCI) to collect plant specimens from around the world for its cancer screening program for ten years until 1982 (Spjut 2006). He first visited Western Australia on his bioprospecting adventures in 1981 when he collected six unnamed species of smokebush (Spjut 1981). At the time there was no published information (known to this author) that detailed the Aboriginal use of these plants in Western Australia. The earliest documentation was a compilation of approximately 100 species used by the Aboriginal people of WA (Reid 1979; Reid and Betts 1979) that forms the basis of a yet to be written Aboriginal Pharmacopoeia.

Later publications (post 1993) mention that smokebush was a common medicine, widely used by the Nyoongar people (Zed 2000). Why the previous silence? Was smokebush to be kept a 'secret from the whitefellas'? Perhaps only because of the publicity and potential violation of Aboriginal lore was the use of smokebush made public. As such it would have been an unwilling revelation ... but essential if the Nyoongar people were to retain 'free access' to this resource without outside non-Indigenous 'patent interference.'

NCI research efforts were directed towards finding antiviral compounds with the hope of stemming the HIV/AIDS crisis during the mid to late 80s. This is when the West Australian 'smokebushes' - *Conospermum* species - hit the headlines with an announcement of the discovery, isolation and synthesis of conocurvone, a highly active antiviral (HIV) compound (see for example, Decosterd, Parsons *et al*. 1993). Conocurvone is a constituent of the roots of one of the *Conospermum* species (not named at the time – possibly for reasons of secrecy).

Without the 'written documentation' of smokebush use, its collection by Spjut and the eager post graduate students from UWA and Murdoch University would appear to have been part of the random collection of the NCI's international cancer screening program which lasted from 1960 to 1982 (Cragg, Boyd *et al*. 1993). 'It's there. We don't know what's in it, so let's collect and study it!' characterises the naive natural products research program of the post World War II decades.

Who owns the stuff? Issues associated with traditional knowledge

Amongst all the activity and enthusiasm surrounding the discovery of conocurvone, there was no mention of Traditional Aboriginal Medicine let alone any consultation with the local Aboriginal population in the areas from which the *Conospermum* samples were collected (Zed 2000). Recent documents arising from the 'Plants for People' project initiative of the Desert Knowledge Cooperative Research Centre state that 'smokebush' was widely used by the Aboriginal people of Western Australia (Smallacombe, Davis *et al*. 2007). The territory in WA in which the 'special smokebush' (Maldayar) is found is Nyoongar country, where the claim is that 'maldayar' is 'good medicine' and has been collected for thousands of years (Zed 2000). Because these traditions were not written down, it is difficult to 'prove' that such knowledge has existed for this time. None of the written sources available to the author published before about 1995 mention 'smokebush' as medicine. Therefore from a 'European' legal perspective it is extremely difficult to prove claims in a court of law.

As Blakeney's paper on bioprospecting and the protection of Indigenous medical knowledge states, it is important to:

> Recognise the value of traditional knowledge and practices of Aboriginal people and Torres Strait Islanders and integrate this knowledge and those practices into biological diversity research and conservation programmes by:
>
> • encouraging the recording (with the approval and involvement of the Indigenous people concerned) of traditional knowledge and practices;
>
> • assessing their potential value for nutritional and medicinal purposes, wildlife and protected area management and other purposes; and
>
> • applying traditional knowledge and practices in ways which ensure the equitable sharing of the benefits arising from their use (Blakeney 1997). A little later,

> Kamal Puri (2000) examined the proposition that traditional or cultural knowledge was a form of intellectual property. He noted that Indigenous people have an holistic perspective that doesn't distinguish between the tangible and intangible. Indigenous knowledge is unwritten (it is preserved in oral traditions) and does not have readily identifiable authors. It is subject to collective ownership and to 'rules regarding secrecy and sacredness'.

To this author's mind, the most important requirement is respect for traditional knowledge and permission from the custodians for the use of that knowledge. Every culture has its 'secret/sacred knowledge' although this appears to have disappeared from the western mindset. One is reminded of the Biblical story of Samson ... where he was invulnerable provided the secret of his strength was not divulged to the Philistines. It was only after he told his wife Delilah, who betrayed him, that he was overpowered and rendered helpless by his enemies (Judges 13: 1-5; 16: 5-20). Another case of sacred knowledge is the formulation of the incense prepared by the Levites and used in the tabernacle worship rites of the Israelites (Exodus 30: 23-38). Do we see a parallel here to certain traditional Aboriginal cultural 'secrets' where disclosure to the uninitiated means the collapse of the meaning and power of that knowledge?

Who's allowed to pick the plants? (Issues of access to resources)

Aboriginal friends of the author in Western Australia have mentioned the restrictions now placed on the collection of plants for their own use. From the mid to late 1990s, they bemoaned the fact that they had to get permission from the (then) Department of Conservation and Land Management (CALM) before they were allowed to harvest their 'bush medicine' and other 'traditional bush tucker' plants. This state of affairs appears to have arisen in Western Australia primarily as a result of the concurvone/smokebush 'furore' that erupted when the NCI, AMRAD Corporation Ltd and the Western Australian Government attempted to stitch up a deal to harvest smokebush, and to develop conocurvone into a marketable drug (Armstrong and Hooper 1994; Boden 1995; Quiggin 2004).

A Perth company, Bio-Gene Bioprospecting Ltd, was the successful winner of a tender to analyse the CALM plant extract library, held at the Western Australian Chemistry Centre. This was announced with considerable fanfare (Government of Western Australia 1999). Surprisingly, the work on conocurvone appears to have been shelved and the promised millions pouring into the coffers of the treasury of the Western Australian government have not eventuated. In the meantime AMRAD in its original form has disappeared.

A Google search using 'conocurvone' as search term resulted in 1350 hits (18th April 2010). Many of these were references to news reports and comment on the discovery of the compound, which was incorrectly described as an alkaloid by *New Scientist* writers (Miller and Dayton 1993). CALM sought to protect Western Australian interests and foster the development of the marketable drug by three measures (Boden 1995):

> 1. Declaring 'smokebush' a protected species (which one/s?);
>
> 2. Ensuring that Australian science was intimately involved in the development of conocurvone;
>
> 3. Ensuring that the community of Western Australia (no mention of Indigenous people) should receive an equitable share of the profits, should the compound be developed into a successful pharmaceutical product.

These measures backfired with the joint AMRAD/ NCI/WA Government 'conocurvone HIV/AIDS cure' project terminated in 2004. Was this done to sidestep the legal issues of cultural knowledge and intellectual property? Whatever the case, there is ongoing research in synthetic medicinal chemistry seeking to 'mimic' the structure and activity profile of conocurvone (Crosby, Rose *et al*. 2008).

Some pointers to a way forward?

It is not possible to give a thorough review of the literature regarding the complex issues associated with bioprospecting and how it impacts on Indigenous knowledge and culture in a short article. Key issues include: the inappropriate Euro-centric concepts of intellectual property; the development of consistent government policy (as opposed to spurts of action); the inadequacy of the public domain concept; extension of 'Mabo' (native title to land) type legislation to cultural and intellectual property rights; and the overthrow of current copyright laws so that Indigenous cultural material could not be exploited (Puri 2000).

The crux of the matter is to be found in a Desert Knowledge CRC scoping project on Aboriginal Traditional Knowledge (Smallacombe, Davis *et al*. 2007). This provides strategies for engaging Aboriginal people and raising awareness of aboriginal traditional knowledge. The summa of this paper is "engagement begins with engagement". This means a real and practical engagement with Indigenous people, not simply a theoretical construct or legal fiction.

Are the presents under the Christmas tree empty?

There is no doubt that the Australian flora is a national living treasure. Biodiversity abounds and must be protected. There are plenty of presents under the Christmas tree. After the enthusiasm of the United Nations Convention on Biological Diversity, it seemed that the beautifully wrapped boxes actually contained gifts of value. To the contrary, Firn (2003) and Macilwain (1998) have argued that bioprospecting for new drugs has delivered surprisingly little. Are they correct in their assessment that the boxes are in fact empty – having promised much but delivered little?

According to Braun and Cohen (2010), between 1981 and 2002, research in natural products accounted for 48% of the new chemical entities reported. This leads one to think the boxes are full! Bioprospecting (and the conservation of biodiversity) are promising ways forward in the search for new medicines.

What has not been done in Australia in the case of the 'smokebush' (and probably other examples) is the engagement of the Indigenous community. Non-engagement of disenfranchised Aboriginal Australians has meant that they look on as others unwrap the presents ... and they are missing out. The way to ensure that the bounteous biodiversity is neither plundered nor squandered is to involve all the 'stakeholders' as recommended by Smallacombe *et al*. (2007). There is plenty for everyone but our legal frameworks need to be far more inclusive and value the cultural sensitivities of all concerned.

Coda

In 1992, Spjut returned to Western Australia to plan a mapping and collection strategy. His report (Spjut 1992) reveals elements of 'cloak and dagger' that raise questions about the propriety of the deal to develop conocurvone into an HIV/AIDS treatment. So, was the 'smokebush' affair an example of biopiracy? I think so.

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Tangled

affection is my lazy perennial,
to soothe the thoughts
I sound gentleness and
visit the masseur.
on the altar of tiredness
the yearning is an annual.

I raised my head in the
sighing wind
seeing cloudiness and sky
and falling leaves
passion rumbled with intransigence
misting heart and vision
intertwined
the sheets became bed linen.

Noel Jeffs,
Alexandria NSW

White Hearse

The wife that was

the future,

a partner, exciting possibility, potential unknown his private world, its public show his
pride
& promise, on his arm, by his side, in his mind his unborn children unborn dreams his mobile home his security authority manhood his
ticket to ride his vehicle his

future

became

an obligation, a nuisance, a cover-up pretence marriage the stifling known familiar territory
an obstacle a hindrance suffocating distance
boredom lies double lives beneath the covers his changed mind secrets smiles a good excuse handy pretext socially attractive still his
pride
& prejudice resentment cash maintenance expensive guilt expansive distance growing children withering bonds fastening cuff links smart successful business cards folded underpants socks hands neatly tied

He walks out of the institution daily
The hem of his unstarched dreams
gathers under a tightly ironed grimace
meanwhile
his heart beats madly
against the fine boned bodice of desire

At the end of the day
he parks his car in her garage

Nicola Scholes,
Toowong QLD