Intellectual property rights, benefit-sharing and development of "improved traditional medicines": a new approach

Merlin Willcox[1*], Drissa Diallo[2,3], Rokia Sanogo[2,3,4], Sergio Giani[4],Bertrand Graz[5], Jacques Falquet[6], Gerard Bodeker[1]

1. Nuffield Department of Primary Care Health Sciences, University of Oxford
2. Institut National de Recherche en Santé Publique, Bamako, Mali
3. Faculté de Pharmacie, Université des Sciences, Techniques et Technologies de Bamako
4. Aidemet ONG, Bamako, Mali
5. University de Lausanne, Switzerland
6. Université de Genève, Switzerland

* Corresponding author: Nuffield Department of Primary Care Health Sciences, University of Oxford, Radcliffe Observatory Quarter, Woodstock Rd, Oxford OX2 6HG

Tel: 01865 289339

Abstract

Ethnopharmacological relevance: Protection of intellectual property rights and benefit-sharing are key issues for all ethnopharmacological research. The International Society of Ethnobiology has produced helpful guidelines on access and benefit-sharing which are widely viewed as a "gold standard" but the question remains how best to apply these guidelines in practice. Difficult questions include ownership of traditional knowledge, making appropriate agreements, and how appropriately to share benefits.

Materials and Methods: We present the case study of the development of an "improved traditional medicine" for malaria in Mali and we report how benefit-sharing was applied in this case.

Results: The knowledge about the selected plant came independently from several families and traditional healers. The IPR approach was to recognise that this traditional knowledge belongs to the people of Mali and was used for their benefit in developing a new "improved traditional medicine" (ITM). The traditional healer whose method of preparation was used, and who collaborated in clinical trials, did not request any financial reward but asked for the ITM to be named after him. The most sustainable benefit for the community was sharing the results of which preparation of which medicinal plant seemed to be the most effective for treating malaria. Attempts at providing a health centre and training a health worker for the village did not prove to be sustainable.

Conclusions: Respect for intellectual property rights and benefit-sharing are possible even in a context where the knowledge is not owned by a clearly identified person or group of people. The most sustainable benefits are intangible rather than material: namely recognition, and improved knowledge about which traditional treatment is the best, how to prepare and take it.

Key words: Intellectual property rights; Benefit-sharing; Improved traditional medicine; Reverse pharmacology

Introduction: the need for new approaches

The need to respect intellectual property rights (IPR) of traditional societies over their medical knowledge is referred to in WHO's Traditional Medicine Strategy 2014-2023 (WHO, 2013), and is a legal requirement of the Nagoya Protocol on Access to Genetic Resources and the Fair and Equitable Sharing of Benefits, which entered into force on 12 October 2014. However there are many cases in which medicinal plant products have been developed without respecting the intellectual property rights of the traditional knowledge holders, or indigenous resource rights.

CASE 1. *Prunus africana*

The case of the *Prunus africana* tree, from Equatorial Africa, illustrates what can happen if there is no attempt to respect intellectual property rights (IPR) or access and benefit-sharing (ABS). The bark of *P. africana* was exploited from the 1960s for use in prostate medication by French and Spanish companies. This resulted in a vast depletion of wild stocks of the species across Central Africa. Had there been consideration given to (a) the traditional ownership of forest resources and (b) the traditional and customary ownership of the medical knowledge associated with the use of the species, harvest rates would have been monitored, local communities could have benefited from royalties rather than as mere bark collectors, and monitoring of the harvest would have been a feature of sustainable production. However, none of this was the case, and *P. africana* stands today as a text book case for the consequences of ABS agreements not being applied – species loss, exploitation of traditional medical knowledge, and exploitation of local labour rather than creation of local microenterprises (Bodeker et al., 2014a).

CASE 2. *Hoodia* & the San People

This second case illustrates that standard patents and ABS agreements can be unhelpful to the traditional knowledge holders. *Hoodia gordonii* is a cactus-like plant that grows primarily in the semi-desert areas of South Africa, Botswana, Namibia and Angola, and used as a food and water substitute by the San People of the Kalahari. The South African Council for Scientific and Industrial Research (CSIR) included *Hoodia* in investigations of edible wild plants in the region. In 1995 CSIR filed an application to patent the active components of *Hoodia* for their appetite suppressant properties (Wynberg and Chennells, 2009). CSIR made an agreement for the San to obtain 8% of payments received from the licensee by CSIR and 6% of royalties from sales of the final product.

This patent was subsequently sold to Phytopharm, a UK-based herbal company, along with exclusive global manufacturing and marketing rights to any related intellectual property. Phytopharm subsequently partnered with Pfizer, who purchased the worldwide marketing rights from Phytopharm for a reported $32 million to develop and market diet pills based on the traditionally known hunger suppressant properties of *Hoodia*. Phytopharm had earned over $10 million while the San were still waiting for benefits (Alikhan and Mashelkar, 2009).

After dropping the development of Hoodia, Pfizer sold the rights back to Phytopharm for a nominal amount. Phytopharm then partnered with Unilever to produce a *Hoodia*-based weight management product, licensed in the EU as a functional food – the SlimFast shake (Wynberg and Chennells, 2009).

Unilever withdrew four years later due to safety and efficacy concerns. Phytopharm then exited the functional food business and returned the patent to CSIR, completing a full circle.

While Phytopharm had earned substantial revenues in the tens of millions of dollars, through research and development funding and the sale of licensing rights, the San had received about 500,000 Rand (US$73,000) over a seven year period from the agreement with CSIR and were reported to be “happy with the arrangement'' (Makoni, 2010). This case highlights that it is possible for a company to keep making money from a product through the development process while the customary owners await benefits.

CASE 3. *Pelargonium*

Another landmark case in the field of traditional medicinal knowledge and IPR is that of *Pelargonium sidoides*, commonly known as the ‘African geranium’. Native to southern Africa, records indicate that *Pelargonium peltatum* (ivy leafed geranium), was cultivated in Europe in the 17th century, having been transported by the Dutch East India Company. Other varieties are recorded as in cultivation and subject to breeding innovations in Europe the 18th century and beyond (Craig, 1993).

In 2007, a series of patents was obtained by Schwabe Pharmaceuticals, a German company, on a method of producing *Pelargonium* extracts. These patents were related to the company’s highly popular treatment for bronchitis, named Umckaloabo, produced from extracts of the root of two species of southern African *Pelargonium* - *Pelargonium sidoides* and *Pelargonium reniforme*. Umckaloabo was 20th of the top-selling over-the-counter remedies in Germany and represented a major source of revenue for the company.

Schwabe’s patent for the extraction process was challenged in 2008 by members of the rural Eastern Cape community of Alice, represented by an African NGO, the African Centre for Biosafety (ACB) and a Swiss NGO, the Berne Declaration, as well as by several of Schwabe’s competitors, including the Swiss plant extract company Alpinamed. The positioning of the case was of one of biopiracy – i.e. illicit appropriation of intellectual property by an international corporation of the traditional knowledge of an indigenous community. The African Centre for Biosafety in South Africa and the Bern Declaration in Switzerland called the patents “an illegitimate and illegal monopolization of genetic resources derived from traditional knowledge and a stark opposition to the Convention on Biodiversity”(Hall, 2013).

Given the long history of Pelargonium use in Europe, it was not a surprise that in 2010 the European Patent Office (EPO), in overturning Schwabe’s patent for extraction, simply noted that this was because “it did not fulfill the inventive-step requirements of the European Patent Convention.” The EPO took a safe path on the grounds of a technical failure in the application process, but also noted that it had considered the “parties’ arguments on other grounds for opposition, and conducted an in-depth discussion of aspects of the biodiversity conventions” (Intellectual Property Watch, 2010). Schwabe subsequently announced the withdrawal of five patents related to *Pelargonium*, which was hailed as a victory against biopiracy by ACB and its partner organisations.

From these examples it is clear that the classic method of patenting cannot easily be applied to the development of phyromedicines. Patents have not protected IPR for companies, and have not

provided benefits for traditional knowledge holders. As African countries develop “improved traditional medicines” (Willcox et al., 2012), new approaches are needed to address the issues of intellectual property rights, access and benefit-sharing.

The International Society of Ethnobiology has produced helpful guidelines on access and benefit-sharing which give good broad principles as well as a set of questions for researchers to review at each stage of the research process (International Society of Ethnobiology, 2006). The ISE Guidelines are widely viewed as a gold standard in the ethical conduct of ethnobiological research and serve as the frame of reference for best practice in applied research projects (Bodeker et al., 2014b).

The question we wish to address in this article is: how best to apply these guidelines in practice? Challenges include the following:

- In the case of traditional knowledge, who is the owner? Is it an individual, a family or a community?
- Is it necessary to protect IPR, and if so, how?
- How to make an appropriate benefit-sharing agreement without raising false hopes? (noting that most research projects on medicinal plants do not lead to a commercial product)
- How to share benefits equitably with communities and traditional healers?

In this article we present a case study of how these questions were tackled in Mali during the development of an antimalarial phytomedicine. The scientific aspects of the research have already been published elsewhere (Willcox et al., 2011a), so this article will purely focus on the handling of intellectual property rights. The translational aspect of almost all ethnopharmacological research is severely challenged by the very issues raised in the paper. The case study of *Argemone mexicana* is an illustration of the problem, tried solutions and lessons learned. We will discuss lessons learned for future similar projects.

Benefit-sharing at every step of a research programme. Case study

Stage one: Identifying the most promising plant

The “retrospective treatment outcome study” of malaria treatments in Mali has been described elsewhere (Graz et al., 2005),(Diallo et al., 2006). Consent was first obtained from community leaders (namely the village chiefs) for the study to take place in their communities. The study team explained that the aim was to develop a new “improved traditional medicine” for malaria in Mali. Secondly, families were asked for verbal consent before interview. They were told that the study team would come back and discuss the research results during meetings open to the whole population and would use the results to develop a new medicine for Mali. Respondents were advised not to share any secret remedies if they did not want them to be used in this way. Traditional Healers were also interviewed about the herbal medicines they use for the treatment of malaria, and were made aware that the plant names would not be kept confidential. Indeed each recipe was also linked to the code representing a healer, so that their intellectual property could be recognised.

Interestingly the plant associated with the best outcomes [*Argemone mexicana* (Papaveraceae)] was used by only 30 out of 952 households (Willcox et al., 2011a) and was only mentioned by 5 of 30

traditional healers in the study area (Diallo et al., 2007). This raises the question as to who owns the traditional knowledge. Clearly it is more than one person, more than one household, more than one traditional healer, and more than one village, within the study area – but it is still a minority of each of these categories. However the "benefit" at this stage was to feed back results to the communities about which treatments seemed to be associated with the best results.

Stage 2: Observational clinical study

For this second stage (Willcox et al., 2007), it was necessary to select a village where the remedy was commonly used. The selected village, Missidougou, had a chief, Tiemoko Bengaly, who was also a traditional healer. He had learned about the use of *Argemone mexicana* from his own grandfather, who had been inspired to use the plant by a dream. He had found it to be effective, so continued its use.

The researchers obtained permission from the Ethics Committee of the National Institute for Research in Public Health, the national malaria control programme, local authorities and village chiefs before commencing the study. Chief Bengaly was a key part of the study team, and was paid an honorarium like the other researchers. The researchers observed patients who came to consult him, and the first inclusion criterion was that Chief Bengaly had diagnosed uncomplicated malaria ("sumaya" in local terms) and accordingly prescribed *Argemone mexicana* decoction. Chief Bengaly prepared the decoction according to his own recipe, which was carefully documented by the study pharmacist. He also decided the doses to be given.

At this stage of the study, the main benefit was to share the results with the community, of the optimal dose and duration of treatment. Other benefits included the presence of a medical team in the village during the study. An agreement was reached that the medical team would offer free consultatons to patients with other illnesses which the healer was unable to treat. The healer's son was also trained as a member of the study team, and after the end of the study, the research team paid for him to be trained as a health care assistant, so that he could provide some basic services such as dressing wounds. Technology transfer and training are recognised as a form of benefit sharing.

Stage 3: Randomised Controlled Trial

This study was done with approval of the national, district and local authorities and with the full consent of the village chief and elders of Missidougou (Graz et al., 2010). A small health centre was built, furnished and equipped with a solar electrical system, so that it could serve as a small health centre for the village after the end of the study. Chief Bengaly and his son were again engaged to be members of the study team. On this occasion, Chief Bengaly delegated to his son the task of seeing patients as a "village health worker", and referring appropriate cases to the study team for inclusion in the study. As before, the medical team provided free consultations and emergency medical care to the villagers. In the process, the medical team also provided additional training to the village health worker. Furthermore, the study team created a medicinal plant garden ("green pharmacy") in the village.

Apart from the immediate medical care, the main benefit to the community of this study was to know that *Argemone mexicana* decoction did indeed seem to be safe and effective for the home treatment of presumed uncomplicated malaria, especially in patients over the age of 5 years, in

whom there were no cases of severe malaria over a 3-month follow-up period (Willcox et al., 2011b). These results were again disseminated to the community.

Stage 4: Isolation of active compounds

There have been attempts to isolate the active compounds, as a marker for standardisation, agronomic selection of the best varieties of the plant, and for quality control (Simoes-Pires, 2009). Laboratory models of disease have many limitations regarding the estimated correlations between animal and human doses and toxicology, the different infectious models or physiologic properties of animals and humans and the endpoints observed. In this case the animal model suggested that the traditional medicine was ineffective, whereas the clinical studies in humans suggested that it is effective. Secondly, the complex mixture in this traditional formulation may have benefitted from synergism between the component compounds. A pharmacokinetic study has been conducted in healthy volunteers in an attempt to discover which compounds are absorbed into the blood stream, but so far this has not yielded results which could explain the observed clinical activity. Therefore it is unlikely that any pure compound will be developed or patented for the treatment of malaria.

Development of an "improved traditional medicine"

However, on the strength of the clinical studies, the Department of Traditional Medicine (DMT) of the National Institute for Research in Public Health (INRSP) decided to develop *Argemone mexicana* as an "improved traditional medicine" (Médicament Traditionnel Amélioré), according to the official guidelines in Mali (Willcox et al., 2012). Chief Bengaly was asked what compensation he would like for the development of his medicine, and he replied that he was not interested in money. He wanted his knowledge to be used for the benefit of his country, but also wanted his name to be remembered. He requested whether the improved traditional medicine could be named after him. The DMT agreed to this, and furthermore presented him with an honorary diploma in recognition of his services to research and development of a new antimalarial phytomedicine.

Prof Rokia Sanogo developed a syrup formulation of *Argemone mexicana* (Sanogo et al., 2014; Sanogo et al., 2012) and was awarded a national prize for this innovation. She gave 25% of the prize money to Chief Bengaly, and the other 75% was shared with staff of the Department for Traditional Medicine. The plants used to make the syrup were harvested from the area where the original clinical studies were conducted, leading to a direct economic benefit for farmers. There is the prospect that this could become an alternative crop for farmers in the future.

Meanwhile, a repeat of the "retrospective treatment outcome study", ten years after the first one in the same study area, has shown that 58% of children with uncomplicated malaria were treated with herbal medicine alone (compared to 24% ten years earlier), and that use of *Argemone mexicana* has increased from 8% to 26% ($p<0.001$) with reported cure or improvement in 100% of cases among those over 5 years old (Graz et al., 2015).

Discussion

Who owns the traditional knowledge?

This question is almost always difficult to answer. In this case, the knowledge of the plant was owned by several families and traditional healers. The use of the same plant for the treatment of malaria has also been reported in other ethnobotanical studies from Mali (Adjanohoun et al., 1981), Benin (Adjobimey et al., 2004) and India (Nadkarni, 1976). The attitude shared by the research team and Chief Bengaly is that this knowledge belongs to Mali and should be used for the benefit of Mali. Respondents to the initial survey implicitly agreed with this as they were advised not to reveal any secret which they did not wish to be used for the development of medicinal plants.

Western legal systems are based on rights of individuals, whereas many African and Asian societies are based more on "collectivism". Many traditional healers keep their recipes secret, but in this example the choice of plant was primarily based on reports from families, with information from traditional healers as a secondary source. On the other hand the method of preparation was provided by Chief Bengaly. It was for this reason, as well as his support and collaboration with the research, that it was decided to honour him by naming the improved traditional medicine after him.

A different approach to the ownership problem would be to consider any traditional knowledge as "commons", freely available in the context of public health. This would leave any single person or group of persons free to keep their secrets, but at the same time publicly available information would not have to be attributed to an "owner" and could be freely used. The impossible complexity of deciding who "owns" traditional knowledge is a good argument in favour of such an approach. In such a model, a pharmaceutical company could use traditional knowledge as a starting point, but could patent only innovations they produce by themselves.

How to make an appropriate benefit-sharing agreement?

Since the knowledge was "given to the country" by the healer, and as such regarded as the property of Mali, and the research team was led by Malians, it follows that no written agreement was made. Furthermore the culture in Mali is largely oral. Many rural people, including the traditional healer, are illiterate. Often they are reluctant to sign papers especially if they do not fully understand them, so a public oral agreement (in the presence of village elders) is preferred. Traditional Malian society considers any declaration given in front of the elders' assembly as the equivalent of a written contract. Nothing can substitute for mutual trust, which can only be built over a period of time and fruitful cooperation.

How to share benefits equitably with communities and traditional healers?

Benefit-sharing has to be context dependent. In this case study, the benefits which reached their intended targets were the free medical consultations for villagers during the study period, the honours and prize money bestowed upon Chief Bengaly, and most importantly feedback of the results. The latter was arguably the most sustainable benefit from this research project. Knowledge given back to the community included: which among their 66 plant species and 166 recipes seems to be associated with the best outcomes; the optimal dose and duration of treatment; and when to seek treatment from a conventional health facility. This knowledge seems to have been of immediate use, as the proportion of *Argemone* users has dramatically increased.

There were unintended consequences, which can be either undesired effects or “benefits”. The traditional healer’s son was trained as a health care assistant, received additional training as a village health worker from the study team, and was encouraged to learn traditional medicine from his father. In spite of this, he decided to leave the village after the end of the study. He said this was because the villagers were not willing to pay him for his services, and he wanted to earn money in order to send his children to a good school. He set up a private clinic in another area and is prescribing modern treatments, reportedly beyond the limit of his competence. He took the solar panels with him from the village health centre, which has fallen into disrepair and is no longer in use because there is no one to staff it. The same fate befell the “green pharmacy” which had been started in the village, because no one took responsibility for it when the healer’s son left the village. Thus attempts at training a health worker and providing a health centre for the community did not prove to be sustainable in this case. Research projects can provide training and donate buildings and equipment, but usually cannot provide salaries for health workers after the end of the projects.

Argemone mexicana is not yet being marketed, so to date there have not been many financial benefits, except for harvesting of the plant for research purposes, and the saving of not needing to use modern medicine for every case of presumed malaria. Marketing of an “improved traditional medicine” will bring benefits in terms of jobs and economic revenue to the farmers who grow the plants and the employees who package the herbs. In Mali improved traditional medicines are produced on a not-for-profit basis so there will be no profits to share. The benefit will be for the people of Mali to have access to an “improved traditional medicine”, and for the farmers who gain an extra source of income from a plant which was previously considered as a pest and an economic cost (because they used to buy herbicides to remove it from cotton fields).

It should be noted that the development of an “improved traditional medicine” is different from classical methods of isolating and patenting a pure compound, which can then be marketed on a global scale to generate large profits. Improved traditional medicines are designed for the local, or at most the national market. The researchers developing “improved traditional medicines” in Mali do so within the context of a publically-funded institute for research in public and do not receive any specific monetary rewards for this work.

Additional intangible benefits include the scientific and clinical validation of traditional knowledge. By creating and ultimately distributing an Improved Traditional Medicine, the research group is also promoting wider recognition and appreciation of the value of traditional medicine, and hopefully making an affordable improved product more widely available.

Global perspectives

In contrast to the cases presented in the introduction, Mali was not trying to patent or “lock up” knowledge about use of *Argemone mexicana*, or to develop an international commercial product. It was trying to develop an improved traditional medicine for use in Mali, while respecting the IPR of the communities and traditional healers from which it was developed.

We must keep in mind the adaptive and dynamic nature of "traditional" knowledge and medicine.. Here we have an exotic weed that has been incorporated into "traditional" medicine in Mali about

four generations ago. The incorporation of this plant into traditional medicines has been observed in several countries.

Although it may seem from this story that granting intellectual property for medicinal plant use is not feasible, the fact is that national, regional and global legal frameworks exist, requiring that free prior informed consent be obtained by researchers from traditional knowledge (TK) holders before any research is conducted. It is also a legal requirement that researchers and traditional knowledge holders enter into fair and equitable benefit sharing arrangements.

The Nagoya Protocol to the Convention on Biological Diversity (CBD) is legally binding on member states. It has, as its overall objective, the fair and equitable sharing of benefits arising from the utilization of genetic resources, which includes appropriate access to genetic resources and appropriate transfer of relevant technologies, taking into account all rights over those resources and to technologies, and appropriate funding. The Protocol applies not only to genetic resources within the scope of Article 15 of the CBD and the benefits arising from the utilization of such resources; it also applies to traditional knowledge associated with genetic resources within the scope of the Convention and to the benefits arising from the utilization of such knowledge (Article 3). This should contribute to the conservation of biological diversity and the sustainable use of its components.

Whether or not the opinion is that this is workable or otherwise, the fact remains that the protocols now must be adhered to under international law. The case story described in this manuscript illustrates an innovative approach for respecting the Nagoya protocol within ethnopharmacological research, without applying for patents or developing a commercial product.

Conclusions

The case study of *Argemone mexicana* illustrates that respect for intellectual property rights is possible even in a context where the knowledge is not owned by a clearly identified person or group of people, and when plants are not being developed for commercial purposes. Mutual trust between researchers and communities are important in making agreements on benefit-sharing. The most sustainable benefits are intangible rather than material: namely improved knowledge about which traditional treatment is the best, how to prepare and take it, and recognition of the healer. The value of knowledge that can be used locally should not be overlooked as a benefit whenever any research is carried out. Secondly the wasted attempts to train a health worker and provide a health centre demonstrate that the provision of technology, although often requested by indigenous communities, is not always an enduring benefit. Further similar case studies are much needed as a Stage 2 to the ISE Guidelines on ethical research practice with Traditional Knowledge, as a way forward in the specifics of applying ethical principles within a field setting.

Acknowledgements

The research in Missidougou (stages 1-3, and the RTO 10 years later) was funded by the Swiss Agency for Development and Cooperation. Testing of antimalarial compounds in the extract was funded by the Medicines for Malaria Venture. Time for writing this article was funded as part of work package 5 of the MUTHI project by the European Union Research Directorate, FP7 Grant Agreement No: 266005.

References

Adjanohoun, E.J., Ake Assi, L., Floret, J., Guinko, S., Koumaré, M., Ahyi, A., Raynal, J., 1981. Médecine Traditionnelle et Pharmacopée: Contribution aux études ethnobotaniques et floristiques au Mali. Agence de Coopération Culturelle et Technique, Paris.

Adjobimey, T., Edayé, I., Lagnika, L., Gbenou, J., Moudachirou, M., Sanni, A., 2004. Activités antiplasmodiales in vitro de quelques plantes antipaludiques de la pharmacopée béninoise. C R Chimie 7, 1023-1027.

Alikhan, S., Mashelkar, R., 2009. Intellectual property and competitive strategies in 21st Century. Kluwer Law International.

Bodeker, G., van 't Klooster, C., Weisbord, E., 2014a. Prunus africana (Hook.f.) Kalkman: The Overexploitation of a Medicinal Plant Species and Its Legal Context. J Altern Complement Med 20, 810-822.

Bodeker, G., Weisbord, E., Diallo, D., Byamukama, R., Sekagya, Y., van ‘t Klooster, C.I.E.A., 2014b. African medicinal plants and traditional medical knowledge: Access & Benefit Sharing in the context of R&D, in: Wambebe, C., Rasoanaivo, P. (Eds.), African Indigenous Medical Knowledge and Human Health.

Craig, R., 1993. HortTechnology 3, 284-290.

Diallo, D., Diakite, C., Mounkoro, P.P., Sangare, D., Graz, B., Falquet, J., Giani, S., 2007. [Knowledge of traditional healers on malaria in Kendi (Bandiagara) and Finkolo (Sikasso) in Mali]. Mali Med 22, 1-8.

Diallo, D., Graz, B., Falquet, J., Traore, A.K., Giani, S., Mounkoro, P.P., Berthe, A., Sacko, M., Diakite, C., 2006. Malaria treatment in remote areas of Mali: use of modern and traditional medicines, patient outcome. Trans R Soc Trop Med Hyg 100, 515-520.

Graz, B., Diallo, D., Falquet, J., Willcox, M., Giani, S., 2005. Screening of traditional herbal medicine: first, do a retrospective study, with correlation between diverse treatments used and reported patient outcome. Journal of Ethnopharmacology 101, 338-339.

Graz, B., Willcox, M., Berthe, D., Ardiet, D.L., Falquet, J., Diallo, D., Giani, S., 2015. Home treatments alone or mixed with modern treatments for malaria in Finkolo AC, South Mali: reported use, outcomes and changes over 10 years. Trans R Soc Trop Med Hyg 109, 209-213.

Graz, B., Willcox, M.L., Diakite, C., Falquet, J., Dackuo, F., Sidibe, O., Giani, S., Diallo, D., 2010. Argemone mexicana decoction versus artesunate-amodiaquine for the management of malaria in Mali: policy and public-health implications. Trans R Soc Trop Med Hyg 104, 33-41.

Hall, M., 2013. The European Parliament is debating a draft biopiracy law requiring industry to compensate indigenous people if it makes commercial use of local knowledge such as plant-based medicines. , EurActiv.

International Society of Ethnobiology, 2006. The ISE Code of Ethics. International Society of Ethnobiology,.

Makoni, M., 2010. San people’s cactus drug dropped by Phytopharm. SciDevNet.

Moolla, A., Viljoen, A.M., 2008. 'Buchu' -Agathosma betulina and Agathosma crenulata (Rutaceae): a review. J Ethnopharmacol 119, 413-419.

Nadkarni, A.K., 1976. Dr K. M. Nadkarni's Indian Materia Medica, 3rd ed. Popular Prakashan, Bombay.

OSISA, 2013. Recognising indigenous rights. Open Society Initiative for Southern Africa.

Sanogo, R., Doucouré, M., Fabre, A., Haïdara, M., Diarra, B., Dénou, A., Kanadjigui, F., Benoit-Vical, F., Diallo, D., 2014. Standardisation et essai de production industrielle d'un sirop antipaludique à base d'extraits de Argemone mexicana L. Revue CAMES, Série Pharmacopée et Médecine Traditionnelle Africaines 17, 15-20.

Sanogo, R., Traoré, F., Djimde, A., Doumbia, L., Maiga, A., Diallo, D., Doumbo, O., 2012. Formulation de sirops antipaludiques à base d'extraits de Argemone mexicana. Pharmacopée et Médecine Traditionnelles Africaines 16.

Simoes-Pires, C.A., 2009. Investigation of antiplasmodial compounds from various plant extracts: *Argemone mexicana* L. (Papaveraceae), *Licania octandra* (Hoffmanns. ex. Roem & Schult) Kuntze (Chrysobalanaceae) and *Syzygium cumini* (L.) Skeels (Myrtaceae), Section des Sciences Pharmaceutiques, Laboratoire de Pharmacognosie et Phytochimie. Universite de Geneve, Geneva.

WHO, 2013. WHO traditional medicine strategy: 2014-2023. World Health Organisation, Geneva

Willcox, M., Graz, B., Falquet, J., Diakite, C., Giani, S., Diallo, D., 2011a. A "reverse pharmacology" approach for developing an anti-malarial phytomedicine. Malaria Journal 10, S8.

Willcox, M., Sanogo, R., Diakite, C., Giani, S., Paulsen, B.S., Diallo, D., 2012. Improved traditional medicines in Mali. J Altern Complement Med 18, 212-220.

Willcox, M.L., Graz, B., Diakite, C., Falquet, J., Dackouo, F., Sidibe, O., Giani, S., Diallo, D., 2011b. Is parasite clearance clinically important after malaria treatment in a high transmission area? A 3-month follow-up of home-based management with herbal medicine or ACT. Transactions of the Royal Society of Tropical Medicine and Hygiene 105, 23-31.

Willcox, M.L., Graz, B., Falquet, J., Sidibe, O., Forster, M., Diallo, D., 2007. Argemone mexicana decoction for the treatment of uncomplicated falciparum malaria. Transactions of the Royal Society of Tropical Medicine & Hygiene 101, 1190-1198.

Wynberg, R., Chennells, R., 2009. Green diamonds of the South: An overview of the San-Hoodia case, in: Wynberg, R., Schroeder, D., Chennells, R. (Eds.), Indigenous Peoples, Consent and Benefit Sharing. Springer Verlag, Heidelberg, pp. 89-124.