

Bio-prospecting in Bhutan: Its Scope and Challenges

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Abstract

Natural products have been an important source of pharmaceutical products, cosmetics, nutraceuticals, fragrances, veterinary products, organic pesticides and many more. Many of the modern drugs that are currently available are the natural products derivatives. Since the diseases are scourging the mankind and its allies, there is urgent need for new drugs. There is also increasing demands for cosmetics, nutraceuticals, fragrances and other organic products. From these perspectives, there is huge potential for bioprospecting worldwide. For Bhutan, while there is a challenge in terms of funding the bioprospecting activities, there are lots of scopes for bioprospecting initiative. This is because; Bhutan is rich in biodiversity and also rich in traditional medical knowledge. These two critical factors supported by the reliable collaborators would make bioprospecting in Bhutan a success. Thus, this paper presents the scopes and challenges of bioprospecting in Bhutan.

Keywords: Bioprospecting; Biodiversity; Traditional medical knowledge; Bhutan.

1. Introduction

Bioprospecting can be defined as the means of systematic finding of utility in natural organisms and making sustainable use of those resources for the benefit of mankind. For example, bioprospecting would mean screening natural products especially medicinal plants for the novel drug molecules. It would also mean adding commercial value to any other natural resources that are of biological origin and utilizing them. So, these may include pharmaceuticals, cosmetics, nutraceuticals, fragrances, veterinary products, organic pesticides and bio-degraders.

Bioprospecting is governed by several international declarations and resolutions like the International Society of Chemical Ecology, The International Convention on Biodiversity held at Rio de Janeiro, in June 1992, International Union of Pure and Applied Chemistry (1996 a, b), The Manila Declaration (1992), Melaka Accord (1994), American Society of Pharmacognosy (1997), The ASEAN Agreement on the Conservation of Nature and Natural Resources, Commonwealth-State Working Group on Access to Australia's Biological Resources(1997), and Trade Related Aspects of Intellectual Property Rights (TRIPS) of the World Trade Organization (Wangchuk, 2004) .

Bioprospecting of natural products for novel drug lead molecules has been the lucrative business for the research organizations and the pharmaceutical companies abroad. However, since bioprospecting for natural drugs involves cross-disciplinary approaches, expensive equipments

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and intensive financial investment, it has been a curse for the poor countries although they are rich in biological natural resources. Bhutan is an example of this. Thus, there is gap between the countries rich in the natural resources and the countries rich in the capital and the technical expertise. These two dipoles, if made to interact and integrate in a positive way, would certainly hybrid the new drug molecules.

This paper presents the scope and challenges of bioprospecting in Bhutan and how to go about it.

2. Why bioprospecting is good for Bhutan?

Although, Bhutan lacks financial resources and research environment, it is rich in culture and biodiversity. Bhutan is recognised as the 10th global hotspots of biodiversity in the world. About 72 % of land is still under forest cover and about 7000 vascular plants and different species of fauna thrive in these luxurious forests out of which about 82 are endemic to Bhutan (Wangchuk, 2004). These endemic species may contain varieties of distinct new bioactive phytochemicals.

About 600 of the vascular plants are used as medicinal plants in the Bhutanese traditional medical system called gso-ba rig-pa. Owing to the availability of medicinal plants in abundance, Bhutan is often referred to as the “Land of Medicinal Plants”. Many medicinal plants such as *Aquilaria agallocha*, *Rawolfia serpentine*, *Ephedra gerardina*, *Taxus baccata*, *Rheum nobile*, *Rheum acuminata*, *Picorrhiza kurroa*, *Nardostachys jatamansi*, *Aconitum* species, *Artemisia* species, *Panax pseudo-ginseng* sub-species *himalaicus* and *Cordyceps sinensis* are in high demand for pharmaceuticals and have potential international market value. Therefore, rich flora and fauna of Bhutan may be hosting cures for many diseases including AIDS, Cancer and other infectious diseases. From that perspective, Bhutan has lots of potential for bioprospecting.

Beside the gift of rich flora and fauna, Bhutan also has rich culture and tradition one of which is the traditional medical system that has existed in Bhutan ever since the 8th century. This medical system uses about 2990 types of medicinal raw materials (Wangchuk et al, 2006) and contains rich ethnomedical information which is useful for bioprospecting. Recent research carried out at the University of Wollongong on two Bhutanese medicinal plants *Aconitum orochryseum* and *Corydalis gerdæ* revealed that the ethnomedical information of gso-ba rig-pa is reliable and factual.

The *Aconitum orochryseum* gave three new bioactive alkaloids which can possibly become an important drug leads (Wangchuk et al, 2007). The extracts and the known alkaloids isolated from *Corydalis gerdæ* gave significant antimalarial activities against *Plasmodium falciparum* and could as well be an important drug leads (Wangchuk et al, 2006). Such study and revelation was just the tip of an ice berg in an ocean full of ethnomedical information. Subjection of Bhutanese medicinal plants, including the component of mixtures, to scientific objectivity and interpretational study would further enhance and validate the Bhutanese traditional medicine. The study would also result in obtaining many novel compounds and unknown new mechanisms of drug action. Thus, our traditional medicine has lots to offer both in terms of primary health care needs as well as in new drug discoveries through bioprospecting the medicinal plants.

The end result of bioprospecting (i.e if prospective and promising lead molecules are discovered in the Bhutanese biological natural resources) could generate enormous income even better than some hydro power projects. The results, if found promising, should be either sold to the private pharmaceutical industries in Bhutan (may take decades to have one) or to the outside companies.

3. What to bioprospect in Bhutan?

The natural world is a rich source of potential lead compounds and discovery of drugs. They include plants, animals, microorganisms, marine products and human biochemistry. Today, extremophiles are considered as important sources of bioactive molecules. In 1973, USA based community pharmacies dispensed the natural product containing prescriptions; 25.2% higher plants, 13.3 % Microbes and 2.7% animals (Wangchuk, 2004). In recent survey, Cragg et al. estimated that 39% of all 520 new approved drugs in 1983-1994 were natural products, and 60-80% of antibacterial and anti-cancer drugs were derived from natural products (Wangchuk, 2004).

Only secondary metabolites are found to possess therapeutic values and many of the secondary metabolites isolated from the natural sources belong to the class of compounds called alkaloids. There are also useful compounds such as flavonoids, terpenoids, steriods and other phytochemicals. They are screened from different sources and their chemical structures are elucidated and those with therapeutic values are synthesized, modified and developed into drugs. Various kind of drugs were discovered in the fields of anti-bacterial, anti-fungal, anti-malarial, antiviral and anticancer agents from plants and microorganisms with the advancement in multi-screening and multi-separation technology.

Therefore, Bhutan should explore its rich biodiversity including plants, animals, insects, insect-fungi, reptiles, amphibians and extremophiles. Most of them are not yet studied. Since some of them dwell in an extreme climatic conditions and harsh vegetation, the probability of discovering new drug leads is high. There are also lots of tshachus (hot springs) and menchus (medicinal waters) in Bhutan and all of them were reported to be effective in treating many types of diseases. Behind the efficacies of such tsachus and menchus, there must be some extremophiles such as bacteria and other agents. These extremophiles has potential to furnish new bioactive molecules similar to the case of the hot spring of Yellowstone National Park in USA (Stewards' Watch, 2000).

4. How to bioprospect?

The two most commonly used search strategies for bioprospecting natural bioactive compounds are:

- a) biologically directed strategies where random approach using high throughput screening is used and bio-rational approach using ethno-botanical and traditional medicines filters are employed.
- b) The other strategy is a chemically directed strategy that involves chemo-rational approach.

The invention of High Throughput Screening and High Efficiency Separation Technologies has enabled the multi-chemical isolation at one go and increased the ground of research manifold.

Different countries based on their disease pattern, the research and drug development activities are heading towards new era in combating diseases by finding many lead molecules in natural products (plants, animal origin and marine sources).

While bioprospecting, the Intellectual Property Rights (IPR) is equally significant. IPR can be described as the law that governs and protects the rights of communities over who should be given ownerships and at the same time who should be accredited for accessing material resources and the information involved in drug discoveries. Therefore, before bioprospecting for novel compounds from the biological natural resources of Bhutan, appropriate IPR laws, regulations, law agencies and agreements should be put in place. This would prevent biopiracy and intellectual piracy.

Intellectual property of any kinds has to be in tangible form. The intellectual property rights over this tangible property can be protected by variety of formal and informal agreements. The new intellectual property, such as new drug, can be protected by both patents and licenses. Contemporary intellectual property law like the Trade Related Aspects of Intellectual Property Rights (TRIPS) of the World Trade Organization, however, permits only the patenting of an identified active principle from a plant, not the plant or folk information relating to medicinal properties of plant. This legislation do not recognizes the right of the indigenous people over equitable sharing of the benefits arising out of their contributions towards innovation. Thus, intangible ethno-botanical information cannot have definite protection of rights and such legislation merely encourages ethnic intellectual piracy.

However, strong and binding agreements on the fair and equitable sharing of the benefits of bioprospecting as well as preservation of the bio-resources should be made and trustworthy collaborating partners identified to prevent such unethical practices. The dossier of traditional knowledge if provided should also be given due credence. All these gestures are necessary to promote long term sustainable bioprospecting through concerted efforts of conservation and protection of the genetic resources. The conservation efforts would invite more reliable inventories of the flora and fauna. Such inventories would help the conservationist and the bioprospectors to determine which plants to be protected based on their availability and distribution. It might also trigger the discovery of new species from the new areas.

5. Where to bioprospect?

Bhutan has rich bioprospecting materials but lacks in research and development facilities as well as qualified researchers in the area of natural product research especially bioprospecting. So probably, primary screening could be done in Bhutan only and for the advanced screening of phy-tochemicals and their activities could be outsourced through proper signage of Memorandum of Understanding (MoU) and legal agreements. There are good Research and Development Laboratories as well as Pharmaceutical companies in Thailand and would be an ideal collaborating country in the region. There are also lots of other countries including USA, Australia, Denmark, Japan and other European countries showing interest in collaborating with Bhutan in the areas of bio-prospecting. At least, till Bhutan gains independence in the areas of natural product research (in terms of facilities and technical know-how), the collaborative approach is the only best way forward to endeavour into bioprospecting.

6. Who should bioprospect?

As of now, there is only one institute well versed and well experienced in natural products and their utilisation. That is the Institute of Traditional Medicine Services (ITMS). ITMS has few qualified and trained personnel in the area of natural products and bioprospecting. Therefore, Research & Development Section of PRU, ITMS could take a lead in bioprospecting and product development activities. If this contradicts with the mandates of ITMS, which is to manufacture quality traditional medicines only, the bio-prospecting initiatives can be taken up by the National Biodiversity Centre under the Ministry of Agriculture.

Another strategic approach to bioprospecting is to establish a government autonomous organization under the banner of “National Bio-tech Laboratory of Bhutan (NBLB)”. This can be easily done by pooling in the equipments and man power that are currently available sporadically spread wide across the departments, organizations and ministries in Bhutan. For examples; ITMS, Bhutan Agriculture and Food Regulatory Authority (BAFRA), Soil and Plant Analysis Laboratory (SPAL), National Environment Commission (NEC) and few organizations have the expensive equipments like HPLC, UV Spectrophotometer, GCMS and AS. However, the equipments available in these above organizations may be underutilized. Underutilized because: a) there is lack of trained human resources in operating those sophisticated equipments, b) the chemicals and reagents are too expensive thereby making the operating and maintenance cost too high to afford, and c) there is too less samples to put the expensive equipments into optimal use. So making those expensive equipments centrally available through a central laboratory set up could avoid wastages of resources and duplication of the related laboratory works. Such kind of national/central Bio-tech laboratory are limited in the region and the fee-based service users can be also explored within the region. This could facilitate the optimal and sustainable use of the laboratory equipments and at the same time could generate the income through user fees system. This income could be used for buying the expensive equipments like NMR, IR, X-ray crystallography. This system is even prevalent in the richer country like Australia and it is most appropriate for Bhutan to have it soon.

7. When to bioprospect?

Having known the potential of bioprospecting in Bhutan, there is need to start immediately.

In fact, bioprospecting has been much talk about topic across the offices and dinner tables by the technocrats, bureaucrats and the politicians. It is high time that these words are put into practice.

8. Conclusion and future direction

In the era of information and communication advancement, the world has become too small that one cannot remain locked forever from the preying eyes of outside world especially the pharmaceutical companies. Similarly, how long and how tight could Bhutan keep its natural resources and ethno-medical information locked? While Bhutan is rich in biodiversity with added advantage of having rich traditional medical knowledge, is it wise enough to tighten up the

regulations and be too conservative on the exploration of our natural resources?. Or could it be much wiser to open up slowly with the changing times and tap these great potential of bioprospecting the natural resources based on the rich traditional medical information? The author would definitely go for the latter and recommend for immediate bioprospecting initiative but with the right and reliable collaborative partners. If the move for bioprospecting is made now, after 10-12 years down the line, Bhutan would be able to realize the benefit from this bioprospecting initiative.

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