Recently there has been a debate in Hawaii about bioprospecting plants as sources of new pharmaceuticals, and the roles of traditional knowledge. The issues are important, although poorly understood by advocates. Most people seem to think that the process proceeds by a researcher simply testing every plant to see what it is good for. However, the truth is that no molecules from plants have been discovered and marketed as pharmaceuticals in the United States in the last 30 years (a period of the most intensive search for drugs in history.) The myth that the next cure for cancer is to be found by searching in a rainforest should be set aside. However, we should not abandon study of traditional medicine, but instead be more realistic about the process and outcomes of research.

Modern pharmacology is built upon a set of observations and predictions about relationships between receptors (often proteins imbedded in membranes) and ligands (any drug or other chemical mediator). The interaction between receptor and ligand results in an event or effect. Pharmaceuticals are selected based upon their actions at this level and our abilities to distinguish positive effects in a range of assays from the molecular to the whole animal level. Therefore, when a drug is administered to a patient, we expect the drug to exert its effect through interactions at receptors (or other target molecules). Although there are drugs that do not work by this kind of mechanism, this is the general pattern of modern pharmacological thought. This causes us to look for a magic bullet with a one to one correspondence between remedy and efficacy.

For decades, the emphasis has been on simplistic collection of as many plants as possible, extraction of their chemical contents, and testing those contents in a wide range of biological assays. After much work, this has proved to be a poor method for identification of new drugs. A more efficient way is to look at how the plants are used by people in traditional communities. This is a difficult task for professionals; we tend to ignore comments of people when they do not correspond to our world view. For example, there are very few patients who enter and leave the doctor’s office with a receptor-ligand mechanism of action in their heads. Over a 10-year period I worked as a pharmacist in a variety of settings. I do not recall any discussions with patients, wherein the receptor-ligand theory was articulated by the patient as a mechanism for the effects of drugs. Instead, patients consistently discussed ideas based upon simple assumptions such as can be seen in the following frequent comments: “if a medicine tastes good it must not be very strong (effective)”; “if a medicine tastes bad is must be strong (effective)”; “if a little bit is good, more must be better”; “I suffer from a chemical imbalance and this medicine balances my system”; “why do I need to take the medication if I feel fine”; and “my body is immune to that antibiotic”. Each of these statements made perfect sense to the patient. Most professionals, however, would dismiss these statements as lacking real information. They find it uncomfortable to work with people who have a different world view, particularly if that view is as different as that of someone from another culture.

As it turns out, there are many different world views about drugs and drug-action in the human population. Commonly, these are articulated within the construct of languages, cultural groups, and religious and philosophical perspectives. Within each of these world views is included a set of logically consistent ideas about how and why people become ill and how to return to a healthy state, often with the assistance of plant-based medications. The study of the logical explanations for how medications work, as understood from a specific cultural perspective, is ethnopharmacology.

**Ethnopharmacology**

Ethnopharmacology is not the search for new drugs from cultural sources. Rather, it is the development of more clear understandings of how, when, where, and why people use their own pharmacopoeia. Ethnopharmacology reveals an entire system of which bioprospectors are unaware.

As a researcher, I have spent the last 15 years exploring the perspectives of professional healers from communities in the Solomon Islands, Fiji, Rotuma, Samoa, Marshall Islands, and Hawaii, trying to better understand the logic behind their selection of plant remedies and why and how they feel particular remedies work. I have learned that it is rare for the logic employed to be consistent with or even close to what I was taught in pharmacy school. However, healers are able to diagnose illnesses in patients, prescribe and administer remedies, and see positive results leading to healthy patients.

**Medicinal Plants in the Laboratory**

Although the pharmacological explanations for selection of a plant as a remedy are not the same across cultures, the effects of molecules within cells are the same. For instance, recent reviews of the roles of plants in the treatment of cancer (such as McClatchey & Stevens 2001) reveal that there is still an important role for plants as sources of ideas for development of pharmaceuticals. With cancer, there are even examples of molecules from plants that have been brought to market such as taxol, since its discovery more than 40 years ago. In order to follow new leads, researchers must first determine how to properly test the information that arrives in the laboratory from other cultures. This is not an easy task. With diseases such as cancer,
it is difficult to tell what is being considered as the same disease in
another culture, and therefore, what remedies from other cultures
might be useful for treatment of cancer.

A number of important problems are faced by laboratory research-
ers seeking to study plant medicines based upon observations of
usage in other societies and the complexity of plant systems. These
include:

• Complexity of traditional remedies (usually several plants, pro-
cessed in complex ways).

• Identification of an appropriate evaluation assay when the logic
for the efficacy is inconsistent with anything in modern medi-
cine.

• Complexity of natural plant systems (usually several molecules
work together to bring about an action.)

• Reactive molecules that are released from plant cells, thereby
profondly changing the chemical contents of a remedy.

• Differences between usage in humans and in-vitro or in-
vivo lab assays. Effects of body processing include degrada-
tion of many constituents, binding of some to proteins or lipids,
concentration of some constituents in specific tissues or fluids,
activation of some constituents, and separation of some con-
stituents from others in ways that may enhance activity only
minimally identifiable in extracts of the plant.

• Even intellectual property rights and ownership of plant re-
sources are important considerations.

Researchers tend to test a plant extract or fraction of a plant.
This is consistent with the goal of identification of a single ligand
that is active at one or more receptors. However, this is probably
inconsistent with the logic of most other cultures, particularly for
complex categories of disease such as cancer.

**Recent Research**

One of the most important plants used by healers in tropical Pacific
Islands is *Morinda citrifolia* (known as “noni” in Hawaii). The plant
is used in combination with other plants to treat a wide range of
illnesses including diabetes symptoms; healing of wounds, bruises,
varicose veins; and treatment of ulcers under the skin and skin les-
sions, headaches, fevers, and topical fungal infections (Dixon et
al. 1999, McClatchey 2002). Most biologists would pass off such a
broad list as not having any common thread, and therefore, not take
the value of the plant seriously. However, recent research conducted
at Louisiana State University by Hornick et al. has shown that noni
juice (produced from fruit grown in Hawaii) inhibits the ability of
breast cancer masses to develop new angiogenic growth and induces
apoptosis in newly formed angiogenic masses. Noni may therefore
be effective in the treatment of some kinds of tumors via reduction
of blood supply to the cell mass and/or promotion of programmed
cell death. With this perspective the same mechanisms could sup-
port other claims for noni such as the treatment of some vascular
disorders and healing of wounds, varicose veins and bruises.

We are fortunate in the case of noni to gain insight from two world
views in understanding its mechanism. In general we need to bring
in more of the traditional knowledge by following more closely
what a traditional healer would do. A model that more accurately
follows would be to:

1. Have a healer prepare a fresh sample as it is intended for use in
a human.

2. If the sample is swallowed, then treat the sample with a “di-
genation” process followed by filtration across a membrane that
simulates the digestive tract filtering effects.

3. If the assay is intended to measure effects within a cell
then a second filter should be used that simulates crossing a
cell membrane.

4. The final product should then be suspended in a solution with
appropriate pH and other characteristics to simulate cytosol of
the target tissue and tested in an appropriate assay that is actu-
ally based upon the healer’s logic rather than assumptions on
the part of the researcher.
In our search for magic bullets that are highly specific, we may be overlooking genuine efficacy that is right in front of us. We need to listen carefully to traditional healers, especially because their message is complex and not easily understood from our world view.

For more information on the Cancer Research Center of Hawaii, please visit our website at www.crch.org.

References

Are you paying a hefty price for your medical malpractice coverage?

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