

MEDICINAL PLANTS IN THE EVOLUTION OF THERAPEUTICS—A CASE OF APPLIED ETHNOPHARMACOLOGY

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Summary

Ethnopharmacology contributes with an interdisciplinary vision to the understanding of human health-seeking behavior. Our interest in this chapter is to provide a brief overview of the contributions made by medicinal plants in the evolution of therapeutics, and to show the development of alternative ways of treatment adapted to culture, social development and constrained economy.

As an applied example, a cost-effectiveness analysis of anthelmintic intervention for community control of Ascariasis: Traditional vs. Pharmaceutical therapy is proposed. The prevalence as well as risk factors of Ascariasis were established in three rural Andean communities near Quito, Ecuador. 754 school-age students were randomly assigned to treatment following a pre-test post-test prospective experiment with two intervention groups and one control group.

The average prevalence of Ascariasis after the first coproscopic test was: 13.89% (95% CI = 11.39% to 16.39%). The effectiveness of treatments was: 12.9% for control group, 47.1% for Traditional treatment (TT), and 94.4% for Albendazole treatment. ABZ doubles the effectiveness of TT, and TT quadruples the effectiveness of the control group (non-treatment).

The cost of doing a blanket treatment (treatment without stool test) to 100 children with TT for a year period in 1999 was US\$ 0.014. The blanket treatment with Albendazole had a cost of US\$ 5.87. Evidently, TT was much more cost-effective if the treatment is provided without taking account of the cost of testing the stools.

The cost-effectiveness of a focused treatment shows that Albendazole becomes more cost-effective due to its high effectiveness. Cost-effectiveness in this study was measured as an incremental cost ratio (ICR). This means that treating the children with Albendazole in a blanket treatment increments the cost of treating them with TT by US\$ 1.52.

The recommendation of the type of treatment depends on the available financial resources. From a practical point of view, nobody repeats four times a year a coproscopic examination, so the blanket treatment can be recommended.

1. Introduction

Health and welfare have always been one of the primary concerns of humankind. Different cultural groups have developed a wide variety of traditional procedures to maintain and recover health, particularly in rural and isolated areas, contributing to improved life conditions for large sectors of the population.

People throughout the ages have orally transmitted popular knowledge and skills to maintain or recover their health, but due to the vertiginous progress associated with firstly the invention of writing, secondly the improvement in communications around the world, and more recently the application of a scientific method for knowledge acquisition and validation in health-related practices, the adoption of traditional

knowledge by conventional (scientific or modern) medicine, is still constrained by lack of reliable and verified information on the practices and utilization of traditional remedies and cures.

The use of medicinal plants as a source of remedies is common to the medical traditions of many cultures. Different groups share the use of several hundreds of common plant species, but there are still other plants considered of medicinal value that remain in the cultural traditions of specific cultures. No systematic efforts have yet been made to achieve the integration of diverse manifestations of traditional medical knowledge, or to facilitate the complementation of traditional and conventional health care systems. As matter of fact, there is an urgent need to collect information on and to identify the best health practices all over the world, and to use them cost-effectively to improve health care delivery.

The World Health Organization (WHO) framework for action incorporates into its strategy on Traditional Medicine (TM) two objectives directly related to its safety, efficacy and quality, as well as to promotion of therapeutically sound use of appropriate TM by providers and consumers.

Implementation of these objectives should maximize the potential that TM offers for improving health status world-wide. It also creates, however, a real demand for expertise and collaboration between authorities, researchers and institutions of diverse nature and missions.

WHO definition of TM includes: "...diverse health practices, approaches, knowledge and beliefs incorporating plant, animal, and/or mineral based medicines, spiritual therapies, manual techniques and exercises applied singularly or in combination to maintain well-being, as well as to treat, diagnose or prevent illness", ethnopharmacology can play an important role contributing to accomplish both objectives proposed by WHO's strategy on Traditional Medicine.

The field of ethnopharmacology has regularly emphasized how medicinal plants were important in the evolution of contemporary western medicine. It has stressed the importance of major plant-derived drugs, and the economic importance of natural products in current conventional medicine.

Our interest in this chapter is to firstly demonstrate how the field of ethnopharmacology contributes with an interdisciplinary vision to the understanding of human health-seeking behavior, and secondly to show the development of alternative ways of treatment adapted to culture, social development and economy. This is a broader view of therapeutics, not limited to the analysis of chemical constitution of remedies.

Ethnopharmacology, as a field for the interaction of several disciplines, relates to culture, botany, pharmacology, health, economics, etc. The classic ethnopharmacological approach focused on the use of drugs derived from medicinal plants as the source of biologically active ingredients used to treat common diseases. Our interest is to underline the practice of ethnobotany made by people of non-Western cultures trying to explain how local (emic) concepts of health and disease, specific

preparation of medicines, and traditional therapeutic recommendations facilitates satisfaction of patient, family and community health needs.

This chapter will provide readers with an overview of the contributions made by medicinal plants in the evolution of therapeutics, not only to the contemporary western medicine pharmacopoeia but, especially, as a contribution to reduce human illness and suffering. Several fields of knowledge such as: anthropology, botany, plant chemistry, pharmacology, public health, parasitology, medicine, statistics, economics and rural life style characteristics are combined in an effort to increase our understanding of diverse cultural manifestations related to the offer and demand of traditional or contemporary health care systems.

As an applied example, this chapter describes the use and effectiveness of a traditional remedy compared to the top conventional therapy used to deal with intestinal parasitism. We emphasize the role of tradition, which maintains for generations the same therapeutic practice (ethnomedicine). We discuss the advantages of using plants as alternative treatments, especially when a community control of a given disease can be facilitated by alternative, effective and low cost therapies.

2. Medicinal plants in the evolution of biomedicine

2.1. Medicinal plants as landmarks in medical history

2.1.1. Ancient times

The history of medicinal plants is essentially the history of mankind itself, every culture and civilization has used plants extensively since prehistory. Seeds and pollen grains found in association with human bones or coprolites showed that a wide number of plants were used in some way by our remote ancestors. Probably the oldest archeological remains of early man are situated in caves of what is now Iraq. Those plants still grow in the region, and indicate that they were important for healing Neanderthal human groups, some 60 000 years ago.

A cultural fact useful to explain what may have happened in the past is the study of several contemporary rural sites in South America, where each ethnic group has an extensive knowledge of local flora, cultivates its own medicine garden, and provides information on the medicinal powers of diverse native plants.

Cultural tradition and personal dedication to experiment with diverse plants can explain the accumulation of knowledge by native people aware of the potential contribution of nature to human's life. That ability also found in wild animals and even in some domesticated animals (cats and dogs), is a faculty used by these ethnic groups habituated to live closed to nature, compared to urbanized people who have lost this capacity, becoming unable to recognize which plants to chose for a natural remedy.

There is no doubt that the earliest drug used as an analgesic was the product of sugar fermentation in solution by yeast (ethanol). Alcohol was produced "when crushed grapes or berries in water were left standing in a warm place", as far back as 6400 BC.

The technique of distillation introduced to Europe by Arabic cultures during the middle ages, enabled alcohol to be concentrated at high levels. Since the very beginning alcoholic beverages became “the wonder drink” capable of producing relaxation, elevation of mood, increased appetite, and release of inhibition caused by social constraints. Later alcohol has been used as an anxiolytic, soporific, hypnotic, analgesic, astringent, bactericidal, and also as a solvent.

Probably several centuries before they were described (300 BC) the opiates were used as analgesics administered as a vapor or given through skin punctures. Morphine, one of the active ingredients of opium was isolated at the beginning of the nineteenth century, other famous principles isolated are codeine, thebaine, papaverine, narcitine and narceine.

The principal effect of opiates is pain reduction and a sense of well-being, but euphoria, as a side effect, leads to development of tolerance and physiological addiction with increasing doses that can ultimately lead to fatal overdosing. Opiates have contributed not only to pain control, but also to understanding of basic pain mechanisms and drug-receptor interactions. Natural or modified opiates act on the central nervous system producing drowsiness, mood changes, mental clouding, and pupil constriction. They also decrease gastrointestinal motility and intestinal secretions, causing constipation.

2.1.2. Arabic and Greek legacies

Approximately 1000 years ago, Baghdad became a recognized focal point of medical learning. Muslim, Jewish, and Christian scribes and scholars cooperated in making available a wealth of texts, by Persian-Mesopotamian, Byzantine-Greek, and Indian traditions.

The theory and practice of medicine in the first millennium was preserved for us in a series of books such as: *The Royal Book of All Medicine* by Ali ibn Abbas al-Majusi (Haly Abbas, d. 994), the *Canon of Medicine* by ibn Sina (Avicenna, d. 1037), as well as other books by Ibn Rushd (Averroes, d. 1198) and Moses ben Maimon (Maimonides, d. 1204), which were also complemented by the clinical observations of Abu Bakr Muhammad ibn Zakariyya or al-Razi (Rasis, d. ca. 925), and by the pharmacology of Yuhanna ibn Masawayh (Mesue, d. 857).

The essence of these medical writings flowed west to Damascus, Cairo, Palermo, and Cordoba. Its incursion into Latin Europe began with the translations of Constantine's of *The Royal Book of Haly Abbas*, titled *Pantegni*, (d. 1087), exerting a strong influence on the first university curricula until a second wave of Arabic works which were translated in Toledo around the year 1250.

The emerging universities of the twelfth century European western culture, received the strong influence of the writings of Hippocrates of Cos (fourth century B.C.) and Galen of Pergamum (2nd century C.E.) translated into Latin, mainly from Arabic translations, but also directly from Greek. The Hippocratic foundations were complemented, possibly by Byzantine teachers before the eighth century, with Galen's "*Art of Medicine*" or "*Articella*".

Medieval medical theory and practice had a considerable change after the adoption of the Hippocratic corpus, whose revitalized attempts to explain disease by natural causes and to base healing on rational principles, proposed a new perspective of therapeutic foundations including an accurate diagnosis and treating the causes behind symptoms. Diet and life style including preventive medicine and personal responsibility for one's health were new ideas. At the same time medieval physicians recognized the inevitability of death and their responsibility to help their patients to a tranquil and orderly departure.

2.1.3. Last century of the second millennium legacy

By the year 2000 several medical systems have been recognized around the world. One of them, the most prevalent in western cultures, also known as conventional medicine or scientific medicine, has developed a large industry of medicine and drugs. Using plants as sources of therapeutic agents has isolated bioactive substances for direct use as medicine, e.g. morphine, digitoxin. Pharmaceutical companies have also produced semi-synthesized drugs of higher activity and/or lower toxicity, e.g. metformin, verapamil, taxol. Medicinal plants have been used as pharmacologic tools, e.g. mescaline, yohimbine; and finally, herbal remedies continue to be prepared as they were prepared during the first millennium, e.g. chamomile, cranberry, garlic, *Ginkgo biloba*, etc.

From a million plant species (angiosperms and gymnosperms) on this planet, only about 6% have been screened for biologic activity, and 15% have been evaluated phytochemically for the presence of alkaloids, flavonoids, triterpenes, etc., but false-positive and false-negative tests often provide results difficult to assess. Nowadays, large pharmaceutical manufacturers and some small biotechnology firms have the ability to screen 1000 or more substances per week using high throughput *in vitro* assays.

In the past, plant extracts were evaluated mainly in experimental animals. Collection and screening *in vitro* and later *in vivo* then became regular practice until the mid 1980s. Then, a new approach using a battery of human tumour cell lines was developed. This led to screening of plants for anti-HIV activity *in vitro*.

Scientific research marked the development of an entire process for drug production: formulating an appropriate proposal, obtaining information on biological extracts, screening extracts, isolating active ingredients, conducting preclinical tests and chemical modification, performing clinical trials, and beginning commercial production. The process would take several bureaucratic and financial steps for an average of 10 to 20 years. The final pharmaceutical product has high costs that are commonly charged to the consumer.

The current trend is to seek bioactive compounds from plants to produce synthetic or semi-synthetic derivatives. At the end of the second millennium the high costs of pharmaceutical production and the unequally distributed wealth in capitalized western society keep large sectors of the world population excluded from the benefits of one of the richest industries.

2.2. Medicinal plants as sources of prototypic agents

Despite these serious inconveniences, scientific research has made great contributions to human health. New emerging diseases, chronic diseases, and resistance to current medicines continue challenging ethnopharmacologic research. At the beginning of the third millennium new products are under research processes. These are a few examples of the titles of recent research projects published in scientific journals (Jan. 2005) as a demonstration of this increasing field of scientific work around the world:

- Studies on pharmaceutical ethnobotany in Arrabida Natural Park (Portugal).
- A search for natural bioactive compounds in Bolivia through a multidisciplinary approach: Part VI. Evaluation of the antimalarial activity of plants used by Isoceño-Guaraní Indians.
- A Chinese herbal medicine Ermiao wan reduces serum uric acid level and inhibits liver xanthine dehydrogenase and xanthine oxidase in mice.
- An *Uncaria tomentosa* (cat's claw) extract protects mice against ozone-induced lung inflammation.
- Cardiovascular effects of the South American medicinal plant *Cecropia pachystachya* (ambay) on rats.
- Anti-fungal and anti-bacterial activity of some herbal remedies from Tanzania.
- Screening of New Caledonian and Vanuatu medicinal plants for antiprotozoal activity.
- Interesting biological activities from plants traditionally used by Native Australians.
- Anti-HIV activities of organic and aqueous extracts of *Sutherlandia frutescens* and *Lobostemon trigonus*

Many drugs used in conventional medicine constitute the outcome of several research studies which have searched for new molecules derived from new and old natural products. The discovery of new drugs stresses the importance of understanding health practices from indigenous cultures, the current use of medicinal plants, and the social-cultural adaptation of human beings to an increasingly competitive pharmaceutical market.

3. Disease Control in a cross-cultural context: a case of applied ethnopharmacology to common intestinal parasitism.

In order to exemplify the feasibility of applying ethnopharmacology as a field of interdisciplinary contribution, this section focuses on a health problem that has been common and widespread since the beginning of human life—roundworm intestinal parasitism.

According to WHO, innovative preventive and control strategies are required to cope with endemic intestinal parasitic diseases. It is also required to demonstrate social and cultural competency and active participation of community members in developing and implementing health care programs.

Since the early 1970s, Latin America has experienced critical conditions as a result of political, economic and ecological calamities. The outcome includes high morbidity and mortality rates and the deterioration of living standards, especially for people in rural areas. The prevalence of parasitism is difficult to clearly establish in rural areas. Clinical research concerning traditional and pharmaceutical treatment of intestinal roundworms has never been conducted.

Intestinal parasitic diseases, especially soil and water-transmitted helminthiasis and protozoan infections, are highly prevalent in developing countries. A quarter of the world's population is affected by *Ascaris lumbricoides*, a nematode worm usually known as roundworm. In Latin America it has various popular names such as: cuicas, bichos, lombrices, parásitos or gusanos, all meaning worms). It contaminates rural and urban areas, from sea level to high altitudes where human life is present. In Latin America a study of 23 countries, made by Crompton in 1989, showed an average prevalence of 25.5%.

The attributed cause of endemic helminthiasis in the Andean Region is the use of raw sewage for fertilizing plantations. Major factors related to ascariasis are: poverty, environmental pollution, poor hygienic habits, and lack of safe systems of sanitation and sewage disposal. In endemic areas the prevalence of ascariasis reaches a maximum between the ages of 4 and 14 years and then persists or declines in adulthood. It is also frequently aggregated in families due to their specific hygienic habits.

Ascariasis is endemic in Latin America. Certain geographical regions are more affected than others. Tropical forest areas are affected with prevalence rates above 60%, while some communities located in rural highlands of the Andean valleys are infected with rates below 40%.

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Biographical Sketch

Fernando Ortega is Director of the Department of Integrated Community Development, President of the Universidad San Francisco Bioethics Committee, and University Professor (Medicine, Nutrition and Anthropology) at the Universidad San Francisco de Quito, Ecuador. Professor Ortega's research and teaching interests are focused in a number of areas. One is integrated community development, where he concentrates on the application of multidisciplinary group actions. He leads students and professionals working periodically in development projects throughout Ecuadorian territory. A second area is international health and rural health internships and rotations offered to medical students around the world. Dr. Ortega shares with international students and faculty the ecological conditions on human life due to the multi-weather territory of Ecuador: tropical rain forest in coastal region of the Pacific Ocean, cool temperatures in the Andean communities of the highlands, and the heat and humidity of the Amazon jungle. A third focus is the study of the Traditional Medicine of fourteen different ethnic groups with a medical anthropological perspective. Finally, another of his interests is the study of human contamination with lead and mercury, events that often occur in Ecuador due to the pre-industrial labor of the population

working in tile glazing and gold mining. Fernando Ortega loves practicing track and field competences, in especially sprinting at high altitude.

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