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Editorial

ETHNOPHARMACOLOGY — A CHALLENGE

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Scientists like Rudolf Buchheim, Thomas Fraser and Rudolf Kobert devoted a great part of their active life to the study of the pharmacological effects of natural products. During the time of exploration and colonialism, they had access to a multitude of crude drugs. In fact, one of the best surveys of these drugs was written during this time by Hartwich (1911). It is to men like these that we owe many of the drugs we use today.

It is questionable if any of these prominent research workers can be regarded as ethnopharmacologists in the modern sense. Truly, they spent decades investigating ethnobotanical materials and their active principles, but they did not carry out field studies among different ethnic groups, nor did they in all cases realize the utmost importance of authenticating plant and drug materials. Whereas, at that time, it took months for dried leaves to arrive in Europe for analysis, it is now possible to take a fully equipped floating laboratory up the Amazon, not only for studies of accurately identified fresh botanical material, but also for the analysis of active components in blood.

Interest in traditional drugs is thus not new but has been spurred in recent years by methodological advances in phytochemistry, a growing number of ethnobotanical studies, and an upsurge of interest in renewable resources and traditional medicine.

Defining ethnopharmacology

The observation, identification, description and experimental investigation of the ingredients and the effects of indigenous drugs is a truly interdisciplinary field of research. The term ethnopharmacology has been used loosely to describe this field (Efron et al., 1967; Schultes and Swain, 1976), but so far little attempt has been made to define the aims and scope of this

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discipline. Ethnopharmacologic research is based on botany, pharmacology and chemistry, but other disciplines have made vital contributions. Based on these considerations, we have recently defined ethnopharmacology as "the interdisciplinary scientific exploration of biologically active agents traditionally employed or observed by man" (Bruhn and Holmstedt, 1982). This study of traditional drugs is not meant to advocate a return to the use of these remedies in their aboriginal form, nor to exploit traditional medicine.

The objectives of ethnopharmacology are to rescue and document an important cultural heritage before it is lost, and to investigate and evaluate the agents employed.

Ethnopharmacological research

Field observations and descriptions of the use and effects of traditional remedies, botanical identification and phytochemical and pharmacological studies, are all within the scope of ethnopharmacology. It is essential, however, that anthropologists interested in ethnopharmacology seek contact and collaboration with experts in botany, chemistry and pharmacology. That such a multidisciplinary approach presents added advantages is not always realized. Even in recent times an anthropologist can give an utterly detailed description of an African poison ordeal without bothering about the chemical composition of the poisonous drink used or even its plant origin. Indeed remarkable in a time that favours teamwork and the involvement of many disciplines!

The first successful multidisciplinary attack on an ethnopharmacological problem was initiated by the French naturalist Leschenault de la Tour in 1803. He collected samples of an arrow poison in Java, as well as detailed first-hand information from the natives about the ingredients and preparation. In France a specimen of the major plant ingredient was studied by the botanist Jussieu who identified it as a *Strychnos* species. Leschenault then gave the poison to Magendie and Raffenau de Lille, who studied the effects in hens, rabbits, dogs and a horse. They observed violent convulsions, asphyxia and death in 5 min and discovered that the chief action was on the spinal cord. This finding is a landmark in pharmacodynamics, since it represents the first time that the action of a poison was shown to act on a specific organ. A decade later the alkaloid responsible for these symptoms, strychnine, was isolated by Pelletier and Caventou. Thus, we have here for the first time an interdisciplinary study starting with fieldwork among natives and continuing with botany, pharmacology and the isolation of the active principle. Later on this was followed by the introduction of strychnine into clinical medicine.

The identification of medicinal plants and other traditional drugs is of course a crucial point, and good ethnopharmacological research can only be based on properly prepared voucher specimens, carefully authenticated by experts. There are many examples in the past, however, of pharmacologists

neglecting this point, only to find that their results are difficult to repeat. Wherever possible, phytochemical studies on medicinal plants should be followed by a careful search for the biological activities of the compounds isolated. When biologically active principles have been found, the findings must be interpreted in the light of the traditional use.

It is impossible, however, to establish a dose-effect relationship unless the original drug preparations (water infusions etc.) are analysed and evaluated chemically and pharmacologically (Malone, 1977; Landgren et al. 1979). As a result we must, in ethnopharmacological reserach, have proper sampling and analysis methods, and this necessity requires close cooperation by pharmacologists, with anthropologists and ethnobotanists on the one hand and specialists in chemical analysis on the other. A recent example from our department of this approach is *Duboisia myoporoides*, used by the natives of New Caledonia as an antidote in ciguatera fish poisoning. Since a water infusion of *Duboisia myoporoides* is used for the treatment of ciguatera poisoning, such an infusion was prepared and the alkaloid content quantitated. The water infusion contains a powerful mixture of nicotine and scopolamine. Prepared in the traditional way, two mouthfuls would equal roughly 50 mg of nicotine and 20 mg of scopolamine. The potential of this preparation in the treatment of ciguatera poisoning became evident when modern knowledge of the poisoning was examined. Based on in vitro experiments with the toxin, two well-known anticholinesterase antidotes have been suggested: atropine and pyridinium aldoxime methiodide. Although they have been used with only moderate success, the recommendation of a mixture of pyridinium and tropane alkaloids is a striking parallel to the native use of chemically similar components.

Aqueous decoctions of *Oldenlandia affinis* are traditionally used to accelerate childbirth by the Lulua population in Zaire. In his capacity as medical missionary Gran (1973) observed increased uterine activity in women receiving these preparations. He also isolated serotonin from the plant. However, the usual decoction from about 100 g of dried plant would not give a higher total intake than about 2 mg of serotonin, and since serotonin is rapidly destroyed when taken orally it could have no action. In in vitro experiments with isolated organs, Gran showed that the increased uterine contractions produced by the water extract also persisted after treatment with methysergide. Therefore another, or several other compound(s) must be the active principle(s). In his research, which is a fine example of modern ethnopharmacology, Gran went on to isolate the active principles and found oxytocic peptides.

Most traditional drugs are administered as mixtures of many components, and with today's knowledge of the many possible interactions between drugs, and between food and drugs, ethnopharmacological research must deal with this aspect too. Additive, synergistic, or antagonistic effects are all possible. Various admixtures have also been shown to affect the bioavailability of pharmacologically active principles.

We believe that pharmacological studies of traditional medicinal agents should be initiated prior to, or in parallel with chemical research and should guide the isolation of active principles. Field observations of traditional therapies and the pharmacological effects in humans should be carried out by trained pharmacologists, and when interesting activity is found, controlled experiments should be initiated (Landgren et al., 1979).

Ethnopharmacology and modern medicine

Recent surveys have shown that the percentage of natural products in the modern drug armamentarium is considerable, estimates varying from 35% to 50%. Almost every class of drug includes a model structure derived from nature, exhibiting the classical effects of that specific pharmacological category. A great number of these natural products have come to us from the scientific study of remedies traditionally employed by various cultures. Most of them are plant-derived, and pilocarpine, vincristine, emetine, physostigmine, digitoxin, quinine, atropine and reserpine are a few well-known examples (Farnsworth and Bingel, 1977).

Evidently, the ethnopharmacological impulse to modern medicine can lead to many novel useful drugs, but modern and traditional uses may be entirely different. For example, the plant material studied at the National Cancer Institute (Bethesda, Maryland) has been collected at random, but the analysis performed by Spjut and Perdue (1976) (summarized in Table 1) shows that if antitumor screening had been guided by the knowledge of medicinal folklore and poisonous plants, the yield of active species would have been greatly increased. In this study, plants were classified as "active" regardless of tumor system or whether the results were obtained from in vivo or in vitro studies. The validity of the data in Table 1 should therefore be further analysed. Another example is the antileukemic activity of vincris-

TABLE 1

PLANT FOLKLORE: A TOOL FOR PREDICTING SOURCES OF ANTITUMOR ACTIVITY?

Plant types	% active[a]
Plant collected at random	10.4
Plants used against cancer	19.9
Anthelmintics	29.3
Fish poisons	38.6
Plants poisonous to man	50.0
Arrow poisons	52.2

[a] Extracts show a significant inhibitory effect in experimental tumor systems (National Cancer Institute, Bethesda, MD) (Spjut and Perdue, 1976).

tine from *Catharanthus roseus* which was found when the plant was investigated because of its folk use as a diabetes remedy.

It is generally accepted that ergot has constituted a gold-mine for finding therapeutically active components (naturally occurring or modified chemically) against many different diseases. It is by no means inconceivable that the cannabinoids may play a similar role in the future. Derivatives are already being tested for various purposes in clinical medicine.

The above data seem to support the conclusion that traditional medicine is a general, powerful source of biological activity.

Ethnopharmacology and traditional medicine

The field of medicinal plants is far from exhausted. The flora of the Amazon has been estimated at 73,000 species. During 30 years of ethnobotanical and ethnopharmacological research in this area, Schultes has collected information on the use of over 1300 species as poisons, narcotics or "medicines". This, and many other treasure-houses of human knowledge are waiting for pharmacologists to take up the challenge (Schultes and Swain, 1976; Perry, 1980).

The ultimate aim of ethnopharmacology is the validation (or invalidation) of these traditional preparations, either through the isolation of active substances or through pharmacological findings. The information gathered about indigenous drugs will permit a feed-back to traditional medicine. Harmful practices can be discouraged, such as the use of plants containing tumor-producing pyrrolizidine alkaloids. Knowledge of active constituents in indigenous drugs may lead to substantial improvements in traditional therapy. In recent years, WHO has emphasized the importance of scientific investigations into indigenous herbal medicines (WHO, 1978). Many Third World countries look upon native medicinal plants as possible additions to the WHO list of "essential drugs", once their value has been clinically proven.

Ethnopharmacology is not just a science of the past utilizing an outmoded approach. It still constitutes a scientific backbone in the development of active therapeutics based upon traditional medicine of various ethnic groups. Although not highly esteemed at the moment, it is a challenge to modern pharmacologists.

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