Ethnobotany and Natural Products: The Search for New Molecules, New Treatments of Old Diseases or a Better Understanding of Indigenous Cultures?

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Abstract: Results of various projects on Mexican Indian ethnobotany and some of the subsequent pharmacological and phytochemical studies are summarised focusing both on chemical-pharmacological as well as anthropological (ethnopharmacological) aspects of our research. We have identified taste and smell properties of medicinal (vs. non-medicinal) plants as important indigenous selection criteria. There exist well-defined criteria specific for each culture, which lead to the selection of a plant as a medicine. This field research has also formed a basis for studies on bioactive natural products from selected species. The bark of *Guazuma ulmifolia* showed antisecretory activity (cholera toxin-induced chloride secretion in rabbit distal colon in an Ussing chamber). Active constituents are procytanidins with a polymerisation degree of eight or higher. *Byrsonima crassifolia* yielded proanthocyanidins with (+) epicatechin units and *Baccharis conferta* showed a dose-dependent antispasmodic effect with the effect being particularly strong in flavonoid-rich fractions. Our ethnopharmacological research led to the identification of sesquiterpene lactones (SLs) like parthenolide as potent and relatively specific inhibitors of the transcription factor NF-κB, an important mediator of the inflammatory process. The inhibitory effect of SLs is very strongly enhanced by the presence of such groups as the isoprenoid ring system, a lactone ring containing a conjugated exomethylene group (α-methylene-γ-lactone) and an α,β-unsaturated cyclopentenone or a conjugated ester moiety. Our work also elucidated the NF-κB inhibiting activity of the photosensitiser phaeophorbide A from *Solanum diploper* (Solanaceae) in PMMA-induced HeLa cells. *Hyptis verticillata* yielded a series of lignans as well as sideritoflavone, rosmarinic acid and (R)-5-hydroxypyrrolidin-2-one and is rich in essential oil (rich in α-pinene, β-pinene and thymol). Other species investigated include *Begonia heracleifolia*, *Crossopetalum gaumerii*, *Epilates mexicana*, *Pluchea symphytifolia* and *Xanthosoma robustum*.

1. INTRODUCTION

Natural product research is often based on ethnobotanical information and many of the drugs used today were developed from medicinal plants employed in indigenous societies. Even more importantly, the study of these resources in order to contribute to better health care in marginalized areas is becoming a central task of modern ethnopharmacological research [1-4]. A major part of the ethnopharmaceutical research in recent years has been directed to a better understanding of the pharmacological effects of individual medicinal plants. Phytochemical studies on medicinal plants are relatively abundant [3]. However, less frequent are studies which combine a phytochemical and a detailed pharmacological approach [5] or studies which systematically explore the health effects of an ethnopharmacopoeia1, i.e. effects produced by using medicinal plants under the conditions as they are prevalent in poorer regions or countries of the world. One of the first of these attempts focused on Aztec medicinal plants and - using an analysis of the pharmacological and phytochemical literature available on selected species—showed that a large proportion of the plants used in this historic culture had the effects the Aztecs ascribed to them [6]. Our own group has contributed to this field through several studies on Mexican2 and Tanzanian

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1 An ethnopharmacopoeia is the totality of plants, animals and microorganisms or any other substances used for medical purposes by a culture (e.g. one of the indigenous Mexican groups). Some of these plants are more important than other ones and it is a core task of ethnopharmacological research to identify the main medicinal products of a culture and to contribute to the study of the plants' pharmacological activity as well as the potential toxicological risks of some of the species used.

2 In the summer of 1982 I came for the very first time to México interested both in its natural and cultural diversity. This interest first led to a thesis on the anthopology of malaria control in México and later to an extended fieldstay studying the medical ethnobotany of the Lowland Mixe in Oaxaca. Subsequently, this resulted in a series of ethnobotanical and phytochemical-pharmacological studies conducted in collaboration with many PhD students. My fascination with México’s enormous diversity has certainly not diminished and we as a team hope that these studies have helped to sustain and to further develop the indigenous medical systems of the lowland regions of México we worked in.
cultures [e.g. 7, 8, 9] and is currently working in Guatemala, Australia and Italy.

The diversity of medicinal plants is very high in a country like Mexico, in which more than 50 indigenous languages are spoken and which is very well known for its biological diversity. There are about 30,000 species of higher plants in México [10]. Each region has different local plant resources and from these a basic group of phytotherapeutics is selected [11, 12, 8]. The gathering and use of local resources is still an important aspect of the phytotherapeutic traditions in many regions of Mexico.

This study summarises some ethnobotanical and phytochemical-pharmacological studies on medicinal plant from several Mexican Indian groups - its "ethnopharmacopoeias" and the detailed phytochemical and pharmacological study of a few of these species. I give an overview of the research since I got first involved in studies about Mexican Indian medicinal plants twenty years ago and highlight some of the outcomes, the limitations of these studies as well as some of the problems encountered. Also in view of the rapid change, which indigenous cultures all over the world are undergoing, the documentation of this knowledge and its detailed ethnopharmaceutical study is urgent and demonstrates the enormous knowledge and adaptability of these cultures. It is only possible to demonstrate that these cultures are the original keepers of such knowledge if it is documented and known to a wider scientific community.

2. ETHNOPHARMACOLOGY: WHAT ARE THE GOALS?

Ethnopharmacology as a specifically designated field of research has had a relatively short history. The term was first used in 1967 as the title of a book on hallucinogens by Efron et al., namely, "Ethnopharmacologic Search for Psychoactive Drugs" [13]. The field is nowadays much more broadly defined: "the observation, identification, description and experimental investigation of the ingredients and the effects of the ingredients and the effects of such indigenous drugs is a truly interdisciplinary field of research which is very important in the study of traditional medicine". Ethnopharmacology is here defined as first proposed by Bruhn & Holmstedt as the interdisciplinary scientific exploration of biologically active agents traditionally employed or observed by man [14, p. 405 -6]. The last definition draws attention to the study of indigenous uses and does not explicitly address the issue of searching for new bioactive drugs (drug discovery). However, the latter issue has been in the core of the public's attention and has been included in the description of the discipline’s goals as it is seen by the International Society for Ethnopharmacology and the editors of the Journal of Ethnopharmacology. These basic goals are clearly expressed in the editorial statement of this Journal (Journal of Ethnopharmacology - inside cover 2002):

"In recent years the preservation of local knowledge, the promotion of indigenous medical systems in primary health care, and the conservation of biodiversity have become even more of a concern to all scientists working at the interface of social and natural sciences but especially to ethnopharmacologists. Recognising the sovereign rights of States over their natural resources, ethnopharmacologists are particularly concerned with local people's rights to further use and develop their autochthonous resources. Accordingly today's ethnopharmacological research embraces the multidisciplinary effort in the:

- Documentation of indigenous medical knowledge,
- Scientific study of indigenous medicines in order to contribute in the long-run to improved health care in the regions of study, as well as
- Search for pharmacologically unique principles from existing indigenous remedies"

Shortly before the start of the 20th century another frequently used term "ethnobotany" was coined by the American botanist William Harshberger. It did not only focus on medicinal plants, but also on other natural products derived from nature like foods, colouring agents, fibre plants, poisons, fertilisers, ornamentals, and oil plants.

This definition helps to avoid a very narrow view of what should be the principal focus of our attention, but medicinal plants have always been one of the main research interests of ethnobotany and the study of these resources has also made significant contributions to the theoretical development of the field [15]. However, these more anthropologically oriented fields of research are beyond the scope of this review. Here took specifically at the situation in México using examples form our own ethnobotanical and phytochemical-pharmacological research which we have conducted since the early 1980s.

Both terms – ethnobotany and ethnopharmacology – have clear limitations with respect to pharmacy’s role in the study of medicinal plants traditionally or popularly used. In order to highlight the role pharmacy as a profession can play in the development of such ethnopharmacopoeias, I have recently proposed the concept of ethnopharmacy, which encompasses not only botanical and pharmacological but also phytochemical [4], galenical, drug delivery, toxicological [cf. 16], clinical, pharmacy practice/anthropological (e.g. [17]), historical [18] and other aspects of research on medicinal plants in popular and traditional medical systems [1].

3. ETHNOPHARMACOLOGY AS COMPARED TO BIOPROSPECTING

One of the most commonly (mis-)used terms in the field of natural product biology has been bioprospecting. In a strict sense it focuses on the development of new drugs and other useful natural products for the huge markets of the North. New potentially highly profitable pharmaceutical products are developed based on the biological and chemical diversity of the various ecosystems of the earth and the research requires an enormous financial input. The research goes from the collection of biogenic samples (plants, fungi, other micro-organisms, animals), to the subsequent analysis
of the biological-pharmacological activities and to the study of the organisms’ natural products to the development of drug templates or new drugs. There can be no doubt that such resources have made significant contributions to the development of, for example, the medicines we use today.

A key process in this search is high-throughput screening systems as the major international pharmaceutical companies establish them. Huge libraries of compounds mostly based on compounds not derived from natural sources (and sometimes extracts) are screened for biological activity against specific targets. Biodiversity derived products are only one of the many sources of material for these test batteries. This serves as a starting point for drug development. Currently some companies envision the screening of 500,000 samples a week against a single target. It thus becomes essential to have an enormous number of chemically diverse samples available (see below).

Another approach focuses on the development of an ethnopharmacopoeia and may best be termed an ethnopharmacological one (see above). Ethnobotanical studies generally result in the documentation of a rather limited set of very well documented useful plants (mostly medicinal, but also those known to be toxic or used in nutrition). In ethnopharmacology an important goal is the development of improved preparations for the use by local people. Thus it is essential to get information on the bioactive compounds from these plants, their relative contribution to the effects of the extract (incl., for example, synergistic or antagonistic effects), the toxicological profile of the extract and its constituents and on improved galenic preparations to be prepared under local conditions. Such studies will, if they are truly interdisciplinary ones, also contribute to an understanding of the cultural meaning and social importance of medicinal and other useful plants.

In restricting ethnopharmacology to the study of indigenous uses I want to draw attention to the fact that an interdisciplinarily defined ethnopharmacological approach needs to develop research strategies for studying indigenous uses and should allow the further development of such indigenous ethnopharmacopoeias and to contribute to a much more detailed understanding of traditional and popular medicinal plant usage.

Research in this field has for a long time focused on the search for pure natural products from such plants. However, renewed emphasis is today put on the extract as an active principle, since, for example, in many cases synergistic effects between various classes of compounds [19] or additive effects of several compounds have been shown. Consequently, the extract has to be considered as the (botanical) drug; which exerts the effects.

Data like the ones presented here not only allow a detailed understanding of the (medicinal) plant use in a culture, but they also form a scientific basis for further developing such indigenous ethnopharmacopoeias. Already 20 years ago it was shown by Trotter [20] and other researchers that a study of the use of the medical resources of a community as well as one of the potential beneficial or harmful effects of the individual medical products used should be a basis for initiating public health measures in order to assure that, for example, toxic substances or plant species are excluded from an ethnopharmacopoeia.

In this paper I want to demonstrate both the scientific importance of an anthropologically focused interdisciplinary research on indigenous medicinal plants and of a detailed phytochemical-pharmacological study of species selected on the basis of such an ethnobotanical approach. In a previous communication we had shown the advantages of a quantitative ethnobotanical approach [7, 8] and this paper I focus on cognitive ethnobotanical as well as phytochemical-pharmacological aspects of our research.

4. ETHNOGRAPHIC BACKGROUND

Our research group has studied the use of medicinal plants in five indigenous groups of Mexican Indians-Maya, Nahua, Popoluca, Zapotec and Mixe. With the first four the methodology was similar, making a direct comparison of the results possible [8].

The data on the Maya were gathered in the communities of Chikindzonot (pop. 1,500), its neighbouring community Ekpetz (800) and Xcocmil (150) that lie south of the city of Valladolid in the southeastern part of the state of Yucatán (for details, see Ankli et al. [7]).

The Popoluca live on the southern and western slopes of the Sierra Santa Marta, a range of volcanoes between the Lake of Catemaco and the gulf shore, southern Veracruz. These volcanoes form the southern foothills of the Sierra de Los Tuxtla mountain range, a region particularly well known for its biodiversity because the holarctic and neotropical floristic kingdoms overlap here. In a recently published list, 2,700 species were recorded, but there are probably at least 3,000 species growing in the Sierra [21 and references therein, 22]. The main community in this region is Soteapan, where most of the research was conducted.

The land of the Mixe extends mostly through the cool and humid mountains of the Sierra de Juarez in the Mexican state of Oaxaca. San Juan Guichicovi is the only Mixe-speaking community in the tropical Istmo de Tehuantepec. It is the principal community (cabecera) in a subdistrict (municipio) of the same name. In 1980, the municipio had 20,000 inhabitants, while the cabecera 5,500 to 6,500 [23, 24, 25]. The Popoluca and the Mixe are linguistically closely related and are-together with the Zoque-considered to be part of the Macro-Mayan language group.

The area of the Zapotecos is adjacent to the one of the Mixe. Forced in the 14th century by Aztec and Mixtec invasions to leave the highland Valley of Oaxaca, the Sierra Zapotecos settled in their present area. The communities we worked with, especially Santo Domingo Petapa and Santa Maria Petapa, are linguistically and culturally isolated from the other Sierra Zapotec groups [26].

Research in collaboration with Nahua groups was carried out in the Sierra de Zongolica, Veracruz, which is part of the
Table 1. Ethnopharmacology vs. Bioprospecting

<table>
<thead>
<tr>
<th>Ethnopharmacology</th>
<th>Bioprospecting</th>
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<tbody>
<tr>
<td><strong>Overall Goals</strong></td>
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<tr>
<td>(Herbal) drug development esp. for local uses</td>
<td>Drug Discovery for international market</td>
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<tr>
<td>Complex plant extracts (phytotherapy)</td>
<td>Pure natural products as drugs</td>
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<td>Social importance of medicinal and other useful plants</td>
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<tr>
<td>Cultural meaning of resources and understanding of indigenous concepts</td>
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<tr>
<td><strong>Main disciplines involved</strong></td>
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<tr>
<td>Anthropology</td>
<td>Biology including very prominently Ecology</td>
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<tr>
<td>Biology (Ecology)</td>
<td>Pharmacology/ Molecular Biology</td>
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<tr>
<td>Pharmacology/ Molecular Biology</td>
<td>Pharmacognosy/Phytochemistry</td>
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<tr>
<td>Pharmacognosy/Phytochemistry</td>
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<tr>
<td><strong>Number of samples collected</strong></td>
<td></td>
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<tr>
<td>Very few (up to several hundred)</td>
<td>As many as possible, preverably several thousand</td>
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<tr>
<td><strong>Selected characteristics</strong></td>
<td></td>
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<tr>
<td>Detailed information on a small segment of the local flora (and fauna)</td>
<td>Limited information about many taxa</td>
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<tr>
<td>Database on ethnopharmaceutical uses of plants</td>
<td>Database on many taxa (incl. ecology)</td>
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<tr>
<td>Development of autochthonous resources (esp. local plant gardens, small scale</td>
<td>Inventory (→ expanded herbaria) economically sustainable alternative use to</td>
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<tr>
<td>production of herbal preparations</td>
<td>destructive exploitation (e.g. logging)</td>
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<tr>
<td><strong>Pharmacological study</strong></td>
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<tr>
<td>Preferably using low throughput screening assays which allow a detailed</td>
<td>The assay is not selected based on local usage, instead high throughput</td>
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<tr>
<td>understanding of the local or indigenous uses</td>
<td>screening systems are used</td>
</tr>
<tr>
<td><strong>Key Problem</strong></td>
<td></td>
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<tr>
<td>Safety and efficacy of herbal preparations</td>
<td>Local agendas (rights) and compensation to access</td>
</tr>
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**Sierra Madre Oriental.** Its area of 1,900 km² lies to the south of 19° N latitude, and is bordered by the states of Puebla and Oaxaca. The area is subdivided according to altitude into three major regions: the cold highlands (tierra fría), temperate intermediate zone (tierra templada) and hot lowlands (tierra caliente).

5. **WHY IS A PLANT A MEDICINAL PLANT: INDIGENOUS SELECTION CRITERIA**

An example of an interdisciplinary approach to understanding traditional and popular medicinal plant usage is the analysis of the reasons for selecting or rejecting a certain plant as a medicine. People in any given region have the chance to select from a large number of plants. Indigenous healers sometimes state "All plants are curative". However, not all species can form part of an ethnopharmacopoeia because there are simply too many to memorise them all. Wherever people go, work or live, i.e. in every ecological zone, there have to be sufficient species easily at hand for making it possible to treat the most common ailments like diarrhoea, stomachache, respiratory problems, and skin infections. Only a well-defined number of plants are selected as medicinal and even fewer are culturally important ones. Ideally one would want to observe as a researcher the discovery of a totally new medicinal plant by members of this society. In reality the plants used have been part of the cultural heritage often for extended periods of time and today the most frequent observation ethnobiologists make about "novel" medicinal plants in an area relate to the adaptation of foreign plants into a culture. Ethnobotanical research shows that we as ethnobiologists are in fact participating in continuing experiments about the usefulness of plants as pharmaceuticals. Some plants are deemed to be very useful and are consequently used much more widely. Other plants were used more frequently by previous generations, but are now becoming less and less important either because the culture now has access to forms of treatment which are considered to be better or because plants with less undesirable side effects have become available. For example, in case of the Lowland Mixe, the sap of *Hura polyandra* (Euphorbiaceae), which acts as a strong purgative but is also known to have strong side effects, has now been replaced by sodium bicarbonate, a chemical readily available in many of the little shops.
Porophyllum ruderale ssp. macrocephalum (Asteraceae) provides an example of how difficult it may be to make clear-cut distinctions between medicinal and non-medicinal plants. The leaves were used for some time in the Mixe community I worked in. In 1988 a healer brought seedlings of the species and used them in the case of undefined convulsions ("ataques"). The species' properties were actively explored and a few years later the plant had escaped cultivation in his garden and became established in a few rural spots. However, the healer no longer regarded the plant to be of any use at all, but considered it "hierba no mas" (just a weed) without any medical properties. In this case the selection of a new plant was based on previous experience of people outside of the community and the decision to drop the usage on the lack of observable effects (as they are defined culturally).

Other interesting examples are the numerous species popularly called "arnica" showing the importance of folk-naming in the transfer of medicinal uses. The name arnica is derived from the European Arnica montana but is today applied to a variety of species, many also with yellow flowerheads and members of the Asteraceae like A. montana. Tithonia diversifolia (Hemsl.) A. Gray is one of the most important medicinal plants of the Lowland Mixe and they use this "arnica" orally against malaria and other forms of fever and topically to treat haematomas and muscular cramps. The species is commonly used by Zapotec, Popoluca and Nahua and is sometimes used by the Maya. T. diversifolia is also known from various regions of Veracruz for treating dermatological conditions. It is native to the lowlands of south-eastern Mexico and Central America but it is not well known in the ethnobotanical literature. Although a tall shrub (2-3 m), in lowland México the plant is often referred to as "arnica" because the conspicuous yellow flower heads resemble the European Arnica montana. This species is a striking example of cultural exchange of information. It seems that the common usage especially in the treatment of dermatological problems is based on a common label - the name 'arnica' used to explain the pharmacological properties of this species. An alternative explanation would be that the five cultures mentioned invented the use independently and independently adopted the same name. This is unlikely given the fact that the usage varies relatively little between the groups [8].

All these data point to the problem of selecting plants as medicines. In indigenous societies plants are selected as a medicine because of certain characteristics like a conspicuous sap, a species similarity to known indigenous medicinal plants, similarity of the plants or some of its organs to a diseases state and the like. An important group of selection criteria identified by our group and independently by John Brett [27] (cf. [28]) are the taste and smell characteristics of possible medicinal plants. Since the selection strategy for medicinal plants cannot be addressed directly we conducted several studies in which we systematically compared the properties of medicinal plants with the ones of those plants, which are not considered to have medicinal properties. These comparative studies with the Maya and Popoluca are based on previous ethnographic research conducted with the Mixe, Nahua and Zapotec. As far as we know, our studies are the first comparing medicinal versus non-medicinal plants with respect to their ascribed properties especially their taste and smell [29, 30].

If a plant has been identified as a potent remedy, its taste and smell properties, visual or other sensual (e.g., texture) characteristics are used both to identify this species, but also demonstrate the usefulness criteria for identifying novel plants, which may be useful as medicines. For example, for the Lowland Mixe of Oaxaca (Mexico), direct access to the natural environment is among other possibilities made feasible by sensory perceptions of plants and plant products. This is interpreted according to cultural expectations. The Mixe judge uses of a plant based on its characteristic smell and taste (see Table 2). These are used in the decision process on whether a plant may be a potential medicinal and for which particular illness it may be used. Generally, astringent drugs (especially the bark of various trees) are valued to treat diarrhoea and dysentery, bitter plants being used as supplementary therapy for these indications. Bitter, aromatic and aromatic-bitter plants are valued in the treatment of gastrointestinal cramps and pain. Cough and other respiratory complaints are treated mostly with sweet, sometimes sour drugs. This form of perception is central to the Mixe's medicinal plant concepts [see Table 2] while the classification based on the humoral 'hot/cold' dichotomy is of minor importance [3]. Taste and smell properties thus open natural resources to human use. Cultural interpretations of the therapeutic results achieved with these plants are additional criteria for deciding whether the use of a specific plant should be continued and for changes in its use profile.

Our key interest here is the relationship between the ethnobotanical data obtained for the individual plants and the secondary plant products (natural products) prominent in each species. It is possible to identify certain classes of compounds, which seem to be positively correlated with the use of plants as medicine, for example, foramins, (bitter) terpenoids and alkaloids and essential oil (see part 6).

Taste and Smell-Mayan and Popoluca

In case of the Maya [7, 29] we looked at plants considered by a single informant to be medicinal and compared them to those, which she/he considers not to be useful as a medicine. During the initial interviews it had become apparent that the Maya have a detailed knowledge of taste and smell properties of the local plants and especially the medicinal ones. The role of chemosensory properties of medicinal plants was compared to those, which are not considered to be a medicine. After completing the documentation of medicinal plants of the communities [7] individual healers were asked to select a maximum of 10

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3 The humoral system of classification is a dualistic system of classification in which humorally hot and cold states form two opposing ends of a continuum. Such classificatory systems are well known especially from highland regions of México and the main controversy centres around the question of the system's origin: Was it brought over by the Spaniards or is it a native American development [57, pp123-127]. According to this concept healing and food preparation are largely based upon the principle of opposites, the humoral theory [58]. The determination of a plant or a plant part as frío ("cold") or caliente ("hot"), may depend, for example, on the habitat and/or season and time of day of growth or collection, on the form of preparation or on analogy in appearance to some aspects of the illness being treated or features associated with wellbeing, (doctrine of signature) but may also be associated with taste and smell properties.
Table 2. Qualities of Medicinal Plants According to Mixe Indian Criteria

<table>
<thead>
<tr>
<th>Qualities</th>
<th>Mixe terms</th>
<th>Example (plant part used)</th>
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<tbody>
<tr>
<td>aromatic (cooling)</td>
<td>xajts</td>
<td>Sipharuna andina (Jacq.)</td>
</tr>
<tr>
<td>astringent</td>
<td>ni'ity</td>
<td>Guazuma ulmifolia</td>
</tr>
<tr>
<td>bitter</td>
<td>ta'am</td>
<td>Calea zacatechichi</td>
</tr>
<tr>
<td>burning</td>
<td>tsu'tsp</td>
<td>Hura polyandra</td>
</tr>
<tr>
<td>fresh (fresco)</td>
<td>nik²</td>
<td>Peperomia pellucida (L.)</td>
</tr>
<tr>
<td>gelatinous</td>
<td>u'ñv</td>
<td>Helicarpus donell-smithii (Rose)</td>
</tr>
<tr>
<td>hot (like chile)</td>
<td>jamuump</td>
<td>Capsicum frutescens (L.)</td>
</tr>
<tr>
<td>hot (like onions)</td>
<td>jajp</td>
<td>Allium cepa (L.)</td>
</tr>
<tr>
<td>sour</td>
<td>xun</td>
<td>Citrus limon (L.) (fruit)</td>
</tr>
<tr>
<td>sweet</td>
<td>pa'ak</td>
<td>Phyla scaberrima (A.L. Juss)</td>
</tr>
</tbody>
</table>

² Also humid, in this context the term refers to a plant which contains large quantities of sap (for example in the stem or in the leaves).

ethnobotanical taxa which according to their knowledge have no medicinal value in their opinion. The healers were next asked about the taste and smell, the humoral and any other properties of the taxa. Since the informants generally did not know any taste or smell properties of non-medicinal species, the informant, the translator and the PhD student conducting the fieldwork (A Ankli) tasted the 10 plants. The healer then gave his opinion on the taste and smell properties of each taxon.

Since the Maya clearly distinguish between bok (smell) and kii (taste) the answers were recorded in two groups: Taste and smell. The majority of the medicinal plants are selected because of taste and smell properties. For example, in the initial interviews on medicinal plants a traditional healer reported that good smelling plants are used against stomachache, bitter tasting plants are applied topically for skin problems and sweet plants are given to strengthen the body and the blood. The reasoning was not always that a plant is a medicine because it has a certain taste or smell property but often that the plant is used for an illness and that it is bitter or astringent, aromatic, etc. This may indicate that the informants do not necessarily see a causal relationship between taste/smell and a medicinal use, but it may also be that this relationship is a covered one.

The description of smell generally was as good, bad, strong or without smell. In explaining the smell properties the informants additionally compared the odour with common ones like the smell of a person, of a lemon or honey or the strong, aromatic smell of Cyperus articulatus L. According to the Maya a strong smell can be favourable or unpleasant. The ways in which the Maya characterise taste and smell of a plant were used in the analysis, i.e. we accepted the criteria as they were stated by the Maya including somewhat ambiguous categories such as "strong" or "bad" smell. Overall, non-medicinal plants were more frequently reported to have no smell or no taste. Medicinal plants on the other hand are more frequently aromatic ("good smell"), while there is practically no difference in the frequency of responses on bad or strong smell. A good (aromatic) odour was mentioned in 50 % of the cases as a characteristic property of a medicinal plant and thus is a sign for a medicinal use, while only 11 % of the reports on non-medicinal plants classified the species as being aromatic and 55% of the reports indicated that the species has "no smell". Therefore, the absence of smell indicates that the taxon is unlikely to have potential as a medicinal plant.

With respect to taste a larger percentage of medicinal plants were reported to be astringent or sweet, while there is no difference in case of the qualities bitter, spicy and acid. For example, it is noteworthy that the informants considered 44 % and 42% of the non-medicinal plants and medicinal plants, respectively, to be bitter. This criterion, therefore, is attributed to a rather large segment of the surrounding flora but seems to be of no direct relevance for the selection of medicinal plants.

If one analyses the specific groups of indigenous uses some interesting patterns become apparent. Sweet plants are clearly preferred for treating respiratory illnesses, 65 % of all use reports in the group "respiratory illnesses" concerning taste properties are to plants which are commonly considered to be sweet. Another important characteristic of the plants used in this group is that they commonly have a strong smell (65 % of all reports). Plants for the treatment of bites of venomous animals, especially snakes, are frequently classified as bitter (71%). Smell is not an important criterion in this group. Women’s medicine is unusual in including a large proportion of taxa which are considered to have no smell (40%) or no taste (57%). Here, too, a large percentage (55%) are considered to have an aromatic smell. For dermatological conditions bitter (64%) and astringent (33 %) as well as aromatic (47%) taxa are preferred. In order to distinguish between the various forms of gastrointestinal illnesses this group was divided into three subgroups: dysentery, diarrhoea and vomiting. For vomiting aromatic
plants are the preferred forms of treatment (61%). Diarrhoea generally is treated with astringent (50%), aromatic (65%) and/or bitter (33%) plants. Contrary to this, the most popular type of plant for dysentery are those which have no or only minimal smell (67%) or show a bitter taste (35%). Pain and fever mostly are treated with aromatic (52%) or bad (43%) smelling plants while no typical taste is important.

Similarly, responses were obtained on the classification according to the humoral system of the plants in the various groups of indigenous uses. Diseases, which clinically may have similar symptoms, can be classified into humorally "hot" and "cold" and their treatment require remedies, which are of the opposing quality.

Typically female disorders are treated with remedies considered to be humorally hot (88%). Pain and fever on the other hand call for cold remedies (74%). A particularly interesting group are the gastrointestinal disorders. Roughly half of all reports in this group are to taxa classified as hot and cold each. But if one looks, for example, at dysentery it is clear that this illness requires cold remedies (96%). On the other hand, diarrhoea and vomiting call for hot remedies. Dysentery is considered to be a hot illness, because of the blood in the faeces. Diarrhoea and vomiting are caused by cold winds, during cloudy sky or by the rain during the rainy season. Consequently these two illnesses are cold and require hot remedies. Inflammatory skin diseases and bites of venomous animals lead to a localised reddening of the skin and rise in temperature and thus require cold remedies. In case of dermatological conditions the main groups distinguished are inflammation and pimples. Inflammation is considered a hot illness whereas pimples are a cold one. The classification of respiratory illnesses is not clear-cut, 53% of the plants are said to be hot and 47% are said to be cold.

The research with the Maya showed that taste and smell are important for understanding medicinal uses and that certain taste and smell properties correlate with specific medicinal uses. However, since each healer selected his species which are used by other healers in the community and, therefore, a systematic distinction between medicinal and non-medicinal plants was not possible.

This line of research was followed in another case study with the Popoluca [30]. In an initial series of interviews we identified taste and smell categories as they are differentiated by the Popoluca healers like w̃ (good smell), caana (sweet taste), tu' n tu' n (astringent) and tam (bitter). We looked at the frequency with which a certain species was classified as having taste or smell in a group of 26 medicinal plants versus 14 non-medicinal ones, selected by the same group of healers. Therefore, in contrast to the previous study there was a consensus between the healers with respect to the plants, which have, and those, which do not have a medicinal use. We were interested in the question whether there is a statistically significant difference between the two groups of plants with respect to the emic taste and smell classification. For this analysis some of the very specific descriptors (smell like mango) of the sensations had to be classified into more common categories like "weak" or "good" taste/smell [30].

All informants (as well as the investigator conducting the fieldwork) tested the plants by chewing them briefly. Overall, we recorded 189 responses for the group of medicinal plants (26 species) and 122 for the group of non-medicinal plants (14 species). As discussed by Leonti et al. [30], not all data were included in the analysis; (i) in the group "medicinal plants", 174 responses were included, whereby only 24 responses (14%) make reference to an indifferent taste and/or smell for the samples tested; and (ii) in the group "non-medicinal plants", 99 responses were included, whereas 57 (56%) refer to an indifferent taste/smell.

In the group "medicinal plants", astringent and bitter taste properties were most frequently mentioned. Fifty-three out of 127 responses to taste qualities referred to astringency and 43 to bitterness, partly due to the fact that plants are frequently used in the treatment of gastrointestinal disorders. In addition, it is noteworthy that in case of the qualities astringent and bitter, the informants showed a high degree of agreement with respect to the indication mentioned. For example, Psidium guajava and Quercus oleoides (bark) are classified as astringent, Aloe sp. as bitter (see Table 2). The latter case is also of interest since it shows that—not surprisingly—the informants also tend to give value judgements about the properties of the species, (it is considered to have a "bad" smell and taste). Remedies for diarrhoea and dysentery are almost always astringent (bark and root), with the exception of Cissampelos pareira root, which is bitter. For example, the bark of Byrsonima crassifolia is commonly used in the treatment of diarrhoea. It is widely used for this purpose in Mexico and is rich in tannins, as are many other species used in Mexico for this purpose (see below). Stomachache and vomiting, however, are treated with aromatic-bitter herbs like Tagetes lucida and Aristolochia sp. [31]. Only 24 (14%) responses in the group medicinal plants indicated an indifferent taste and/or smell for the samples tested. On the other hand, 60 (59%) responses of the 102 answers in the group "non-medicinal plants" are to an indifferent taste/smell.

Bitter plants are considered to have a strong impact on the body and as being somewhat risky in their use because of a possible overdose. Plants or plant parts with bitter properties (like Calea ternifolia (syn.: C. zacatechichi)) are generally used to treat pain of the body, e.g. of the skeletal-muscular system and stomach-ache. "Bitter" is associated with the humoral system and perceived as being hot, having a warming effect. Decoctions and tinctures against cough are composed of sweet plants (Lippia dulcis, Bougainvillaea sp., Eucalyptus sp.), and often artificially sweetened with sugar or honey. This concept may be derived from the Spanish influence.

For the Popoluca taste and smell are among a group of mnemonic aids used to recognise and remember medicines. Another example is the shape of a plant. In this case plants or plant parts looking like a specific human organ are selected as medicine. Peperomia sp. leaves look like ears and are therefore used against earache A more complex
example are species which symbolise the pain, the symptom and the affected organ. The thorn-bearing vine of *Serjania mexicana* symbolise the pain of the urinary pathway and its white latex the white pus of gonorrhoea [30].

These two studies with the Maya and Popoluca show that an understanding of the indigenous concepts used to distinguish medicinal from non-medicinal species is of considerable heuristic value. The perception of the secondary plant products by tasting and smelling them yields culturally defined clues about a species potential value and helps to distinguish between used and non-used plants. Therefore, plants are neither selected at random nor are they selected based on purely ‘abstract’ criteria like the hot-cold system. Taste and odour characteristics of medicinal plants and the labels applied to them (astringent, bitter, aromatic, etc.) include, or encode, considerable information about the groups of illness(es) a particular phytopharmaceutical is best used to treat [cf. also 29, 30].

From a phytochemical-pharmacological perspective such information provides valuable clues about which plants may be of particular interest for further studies. Smell and taste often characterise typical groups of natural products. This is not only essential for the recognition and selection of medicines but can also help in explaining the pharmacological effects of a species. For instance astringent plants, which contain polyphenols, are used against gastrointestinal disorders and dermatological problems and their pharmacological effects can partly be explained based on the characteristic groups of natural products present in the species (see the species-specific discussions below, part 6). Many of these chemical substances, for instance essential oils in aromatic herbs or the polyphenols of astringent plants, have a positive health effect. Such a clear-cut connection exists for a few classes of compounds. Bitter tasting compounds, on the other hand, belong to a large variety of groups of natural products and therefore no specific pharmacological conclusions can be drawn from the information on the bitterness of a plant. On the other hand, since these data do not allow the quantification of the relevant groups of natural products, no definite conclusions on the physiological effects of the species can be drawn. However, such information has provided essential leads for selecting species for further phytochemical and pharmacological studies. We used such ethnobotanical criteria (together with quantitative data as discussed in [8, 32] and chemotaxonomic information for selecting species for the studies as they are described in the following section.

The selection of plants as medicines is based on pluralistic concepts and is not just one system, which forms a unifying single theory. In these two examples we worked with the specific sensory properties of a plant, like smell, taste, colour, form and texture. These presumably are one of the first criteria in selecting a plant as a medicine and serve as a mnemonic aid for recognising the botanical drug. For the continued use as a medicine, it must show a positive health effect as it is interpreted culturally. A study on the classification of useful plants based on taste and smell properties in other cultures especially from Central and South America are urgently needed. Such studies would provide empirical evidence for the importance of such classificatory systems on a broader scale. It will be also of interest to look at the development of classificatory systems during larger time periods to observe changes in the systems. Plant selection is a continuous and complex process and both from an anthropological as well as from a natural science perspective; it would be of interest to focus on the "career" a specific plant has from some initial observation of an effect or its selection based on the species characteristic to a wider or more restricted usage of such a plant or even the discontinuation of its use.

### 6. PHYTOCHEMICAL STUDIES OF SELECTED MEDICINAL PLANTS

Subsequent to such anthropologically oriented studies selected species were studied in a series of primary *in vitro* and occasionally *ex vivo* screens. The ethnobotanical studies indicated that plants used for gastrointestinal condition as well as for infections and inflammatory skin problems were particularly important in the cultures we worked with. Prior to initiating phytochemical studies we conducted a screening of selected species from these cultures (e.g. [33, 34, 35]). Preferably targets which are of direct relevance to the conditions treated by the healers were used. Consequently our research concentrated on species particularly active in these primay screenings. The overview in the following provides a summary of studies conducted by at the research group of Prof. Otto Sticher (Zurich, CH) and our group at the University of Freiburg (led by Prof. H. Rimpler).

#### 6.1 Species Used in the Treatment of Gastrointestinal Disorders

Ethnobotanical research in *San Juan Guichicovi* (Lowland Mixe) resulted in the documentation a large number of species used in the treatment of gastrointestinal disorders. H. Rimpler and co-workers have for many years been interested in the phytochemistry of European tannin containing botanical drugs especially those used for the treatment of gastrointestinal illnesses. A logical expansion of this research were studies on two of the Mixe Indian plants known to be in previously uncharacterised tannins: *Guzuma ulmifolia* and *Byronima crassifolia*. These two plants were selected from about 10 species collected during the late 1980s, which are traditionally used by the Mixe for gastrointestinal diseases [23].

*Guzuma ulmifolia* is used by the Mixe (ëëk) and less frequently by the Popoluca (ëkë) for diarrhoea. Because of its common name and similar uses it may well be one of the truly "traditional" medicinal plants used by both groups since the times when they still shared a common territory and spoke a common proto-Mixe-Zoquean language. The crude ethanolic extract from the bark was assayed for antisecretory activity using rabbit distal colon mounted in an Ussing chamber as a model for electrophysiological ion transport. Cholera toxin-induced chloride secretion was completely inhibited if the extract was added to the mucosal bath before the toxin, suggesting an indirect effect of the extract on secretion by interaction of the toxin with constituents of *G. ulmifolia*. The active constituents are
procyanidins with a polymerisation degree of eight or higher [40], while smaller procyanidins have a weaker effect. The extract and the fraction rich in polymeric proanthocyanidins was inactive if the colon was stimulated with PGE2, suggesting that the tannins do not form a ‘protective layer’ by precipitating proteins on the epithelial surface of the gut as it had been postulated frequently without any empirical evidence. Instead, the study makes it likely that tannins interact with toxins, which are frequently present in the GI-tract during episodes of diarrhoea. Recently a methanol-dichloromethane extract from a Panamanian collection of the bark was also shown to inhibit the (3H)-ATII binding (angiotensin II AT1 receptor) in vitro by more than 50% [56].

*B. crassifolia* (locust berry tree) is called tax in Mixe or nanche in Mexican Spanish. Uses both for gastrointestinal disorders especially diarrhoea and dermatological problems like skin infections are recorded [23]. It also is an important medicinal plant for treating gastrointestinal problems with the linguistically closely related Popoluca of Veracruz, where it is the most important medicinal plant in the group gastrointestinal illnesses [43], the Isthmus Sierra Zapotecs [41] and, as reported by Berlin and Berlin [37], the Tzeltal and Tzotzil of Chiapas. Bejar and Malone [38] reported in vitro spasmogenic activity of an extract of the bark. The extract possesses antibacterial activity against *Staphylococcus* sp., *Salmonella typhi* and other pathogenic bacteria [39]. Geiss et al. [40] isolated proanthocyanidins with (+) epicatechin units from the bark of this species. Two trimers, one known and four novel dimers, as well as the monomers (+)-epicatechin, 3-O-galloyl-(+) -epicatechin and catechin and gallic acid were isolated. No detailed pharmacological studies of this species have been conducted so far. The isolated tannins may be of relevance in the context of the ethnobotanical reports on anti-diarrhoeal activity. However, this contradicts the report [38] on spasmogenic effects of an extract.

Weimann and Heinrich [41] studied the medical ethnobotany of the Nahua of the Sierra de Zongolica in the Mexican state of Veracruz. Again gastrointestinal disorders are a common problem in this region. Mostly they arise in form of diarrhoea and dysentery with colic and are caused by infections of the intestine with amoebas, bacteria and viruses. 203 different species were cited as medicinal. 72 species with 222-recorded use reports are used for gastrointestinal disorders. The Nahua use *Baccharis conferta* (aerial parts, escobilla china) in the treatment of a variety of gastrointestinal illnesses especially diarrhoea associated with gastrointestinal cramps.

The aerial parts were investigated phytochemically and pharmacologically using the guinea-pig ileum assay as a model [42]. The crude ethanolic extract showed a concentration-dependant antispasmodic effect with the effect being particularly strong in flavonoid-rich fractions. Several flavonoids including apigenin-4',7-dimethylether, naringenin-4',7-dimethylether, pectolinaringenin and cirsimaritin were isolated, while others were identified in complex fractions by GC-MS. The flavonoids play an important role in the antispasmodic activity of this indigenous drug. Additionally oleanolic acid and its methyl ester as well as erythrodial were isolated. Oleanolic acid-methylester shows weak antibacterial activity against *M. luteus* and *E. coli* (20 µg/spot in a TLC assay). The phytochemical as well as the pharmacological data provide some evidence for the use of this plant in the treatment of gastrointestinal cramps.

*Plucheia symphitifolia* is an important medicinal plant used by the Mixe in the treatment of diarrhoea, intestinal parasites, and externally against infections of the ear. The aerial parts yielded six caffeoylquinic acids, including 1,3,4,5-tetra-O-caffeoylquinic acid and 1,3-di-O-[3,4-bis-(3,4-dihydroxyphenyl)-cyclobutane-1,2-dicarbonyl]-4,5-di-O-caffeoylquinic acid (1) and two flavones. The pharmacological effects observed were relatively weak: the aqueous extract had antibacterial and antisecretory effects, the lipophilic extract showed anthelmintic activity and the dicaffeoylquinic acid derivatives contribute to this activity to varying degrees [43].

6.2 Anti-Inflammatory Natural Products from Mexican Indian Medicinal Plants

Inflammatory skin conditions especially those due to microbial infections are extremely common in rural regions of Mexico and this led us to investigate the anti-inflammatory effects of selected plants from the ethnobotanical collections. Again, a screening for biological activity of 10 - 30 plants collected in larger quantities in the respective regions was followed by a detailed phytochemical study of a few taxa.

*Hyptis verticillata* (Lamiaceae) is used medicinally by the Mixe Indians of Oaxaca (Mexico) to treat gastrointestinal disorders and skin infections. Similar uses are reported from other parts of Central America and the Caribbean. One new and 6 known lignans [hyptinin (2), dehydropodophyllotoxin, dehydrodesoxypodophyllotoxin, 4'-demethyldesoxypodophyllotoxin, podophyllotoxin, podorhizol (3) and epipodorhizol (4) as well as sideritoflavone, rosmarinic acid and (R)-5-hydroxyppyrrolidin-2-one were isolated from *Hyptis verticillata*. The essential oil contains as main components...
α-pinene, β-pinene and thymol. The essential oil, (R)-5-
hydroxypropyridin-2-one, as well as rosmarinic acid and
dehydropodophyllumotoxin (and presumably also other lignans)
counter to the antibacterial effects of *H. verticillata* [59].
Rosmarinic acid showed significant capillary stabilising
effects in an assay, which uses the chorion allantois
membrane of incubated hen’s eggs (HET-CAM) as a model.
In the HET-CAM-assay anti-inflammatory effects, the
inhibition of the permeability of capillary systems and
capillary stabilising actions are measured. The crude extract
of *H. verticillata* was applied onto the chorion allantois
membrane (CAM) at several concentrations and delayed the
irritation phenomena injection, haemorrhage and lysis
significantly. Sideritoflavone inhibited prostaglandine
synthase to a significant extent and had antisecretary effects.
The cytotoxicity of the aqueous extract, as demonstrated
using KB and HT 29 cell lines, may be of toxicological
relevance in cases of internal application [59].

![Chemical Structures](image)

In 1996 we initiated a collaboration with Prof. Lino
Schmitz (then in the University of Freiburg, Germany, now
at the University of Bern, Switzerland) focusing on a much
more specific target of the inflammatory cascade: NF-κB-
nuclear factor kappa B. The promotion of inflammatory
conditions and the initiation of the innate immune response
require the synthesis of many special effectors proteins.
Numerous signalling cascades have been elucidated,
involving as one of the last steps the activation of inducible
transcription factors that bind to the promoter regions of
their respective genes. Such targets include the genes for
adhesion molecules (chemokines) and cytokines (TNF-α,
interleukins). NF-κB is one of the principle inducible
transcription factors in mammals and has been shown to
play a pivotal role in the mammalian innate immune
response [44] and chronic inflammatory conditions such as
rheumatoid arthritis [45]. The signalling mechanisms of NF-
κB involves an integrated sequence of protein regulated
steps and many are potential key targets for intervention in
treating inflammatory conditions.

The most widely published classes of natural products
cited as inhibitors of NF-κB are various groups of
diterpenoids and sesquiterpene lactones (SQL) [46].
Ethnopharmacological studies with medicinal plants used by
the Mixe and Nahua first yielded promising NF-κB
inhibitory activity associated with SQL [33, 34]. Band-shift
experiments identified the ethanolic leaf-extracts of
*Artemisia ludoviciana* ssp. *mexicana*, *Calea zacatechichi*,
*Polynnia maculata* and *Tithonia diversifolia* (all rich in
sesquiterpene lactones) as inhibitors of NF-κB down to a
concentration of 20 µg/ml. We next studied the
sesquiterpene lactones isohelenin and parthenolide well
known from other members of the family which prevented
NF-κB activation completely as low as 5 µM. Treatment of
HeLa cells with leaf extract of *A. ludoviciana* ssp. *mexicana*
or isohelenin or parthenolide prevented the induction of
transcription on the IL-6 promoter. These experiments
identified the eudesmanolide and germacranoide type of
sesquiterpene lactones as potent non-antioxidant inhibitors
of NF-κB. All plants active in the NF-κB assay also
showed a delay in the onset of capillary reactions of the
allantois membrane in a physiological model for anti-
inflammatory activity, the HET-CAM assay. Our studies
and studies by M.L. Schmitz and collaborators indicated
that the inhibition of NF-κB activation is a class-specific
activity and that the lactone function conjugated with an
exomethylene group in α-position is essential for the
activity [47,48]. Many more recent reports of inhibitors
within this class varying widely in their MIC values for
inhibiting NF-κB. These differences may be accounted for
by varying assay techniques and in the structural diversity of
SQL and, as such, various structure/function activities can
be identified. The inhibitory effect of SQL is also very
strongly enhanced by the presence an isoprenoid ring system
[47] and an α,β-unsaturated cyclopentenone or a conjugated
ester moieties. The presence of such groups in SQL has been
significant in potent inhibitory activity against iNOS-
dependent NO synthesis monitored directly [49] and a large
number of other biochemical targets. The alkylation activity
of many of its members could explain its high activity and
cytotoxicity. Sesquiterpenes as a class, although structurally
diverse and with many associated therapeutic uses, do
possess unspecific toxicity and presumably this will
preclude any useful medical application [50]. However, the
studies provide exciting scientific evidence explaining a
hitherto not biochemically understood activity of many
SQL-containing Asteraceae used in indigenous and popular
medical systems all over the world.

*Solanum diflorum* Vell. (Solanaceae) is used in the
treatment of erysipelas, local swellings, oedema and fever by
the Istmo Sierra Zapotec Indians of Oaxaca, Mexico. The
ethanolic crude extract (2) of the leaves showed strong
inhibitory activity on NF-κB activation in EMSA shift
experiments at 100 µg/ml. Similarly another member of this
genus - *Solanum lanceolatum*, used to treat local infections,
wounds and "espinilla" showed weak inhibitory activity at
the same concentration. Bioassay guided fractionation led to
the isolation of a fraction mainly composed of phaeophorbid A (fraction P). In addition, lutein, as well as four sterols (cholesterol, campestrol, stigmasterol and β-sitosterol) were isolated. Since it is well known that phaeophorbid acts as a photosensitiser, it was of interest to investigate whether this compound has cytotoxic effects after exposure to light with a wave length >600 nm. After incubation with 3 μg/ml of fraction P for 25 and 55 min, respectively, the cell cultures were exposed to day light for three min. Cells exposed to light showed a complete loss of cell function and were apoptotic, while untreated cells and cells treated with phaeophorbid A but not exposed to light showed no sign of apoptotic processes even after 24 h (data not shown). Since it is impossible to conduct the experiments for NF-κB inhibitory activity under complete exclusion of light the "inhibitory" effects of this compound have to be interpreted with caution. On the other hand phototherapy using photosensitzers is currently discussed, for example, as a therapeutical option especially in the topical treatment of cancers [55].

The crushed aerial parts of Peperomia pellucida (Piperaceae) are popularly used in the treatment of inflammatory dermatological problems (Lowland Mixe) and of various kidney diseases (various cultures of the Caribbean). The ethanolic extract showed an in vitro inhibitory activity on cyclooxygenase (COX 1) and in vivo activity in the HET-CAM assay. Using a bioassay-guided fractionation procedure with COX 1 activity as a lead resulted in the isolation of linoleic acid and α-linolenic acid. Fatty acids are natural substrates for cyclooxygenases and lipoxygenases and are known as competitive and relatively potent inhibitors of both groups of enzymes. The isolation of two fatty acids as inhibitors of cyclooxygenase may therefore be of physiological relevance, but further data on the resorption of these compounds under in vivo conditions (e.g. through the skin) and on their concentration in the indigenous preparations, are required before such claims can be substantiated. Additionally the cation content of the water fraction, obtained after elution with hexane, ethylacetate, ethanol and water from a Celite® column, was determined. The contents of Na, K, Ca and Mg represents roughly 25 % of the water fraction or 13 % of the crude extract. The high content of K (7.7% of the crude extract) and the low content of Na (0.5 %) are very notable. A high content of K⁺ was reported for Piper sanctum, but no data for the genus Peperomia had previously been available: It is well known that medicinal plants which are used as diuretics often have a high content of K⁺ (e.g. Betula sp. or Orthosiphon aristatus with 3 % K) and are known as saline or diuretics. Obviously pharmacological and/or clinical studies and studies using an aqueous infusion will be necessary in order to better understand the pharmacological basis of the indigenous claims, but the phytochemical data gathered so far corroborate the indigenous uses in urology [51].

6.3 Studies Focusing on Antibacterial and Cytotoxic Activity

The roots, rhizomes and petioles of Begonia heracleifolia are used by the Zapotecs and Mixe for a variety of dermatological conditions including wounds, local skin infections (like acne), but also for rheumatism and pain. Frei et al. [52] isolated six known curcumbatins including curcumin B (5) and D (6) and their two glucosides with cytotoxic effects on KB, 3T3 and OC3 cells from Begonia heracleifolia (Begoniaceae). In two further studies by the research group of O. Sticher in Zurich on medicinal plants used by the Isthmus Sierra Zapotecs for dermatological problems eight antibacterial sesquiterpenes were isolated from the aerial parts of Epaltes mexicana (Asteraceae) [53], and four hydroxysterols with antibacterial activity as well as two diols were obtained from the rootstock of Xanthosoma robustum (Araceae) [54].

Crossopetalum gaumerii (Celastraceae) is used by the Maya of Yucatan. A piece of root is chewed and the pulverised root is mixed with water and put on the wound of a person who was bitten by a snake. The decoction is also used orally for diarrhoea. Ankli et al. [31] isolated four cytotoxic (against KB-cells) cardenolides-securigenin-3β-O-β-6-deoxyguloside (7), 19-hydroxy-sarmentogenin-3β-O-β-6-deoxyguloside (8), sarmentogenin-3β-O-[α-allosyl-(1→4)]-β-6-

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**Diagram 6.3:**

- **Diagram 6.3.1:** Structure of β-6-deoxygulosyl-1-O-hydroxy-cholesterol (7)
- **Diagram 6.3.2:** Structure of β-6-deoxygulosyl-1-O-sarmentogenin (8)
deoxyalloside] and securnogenin-3β-O-β-[α-allosyl-(1→4)-β-deoxyalloside], and terpenoids (the diterpene 3,15-dihydroxy-18-norabieta-3,8,11,13-tetraene and the triterpene 2,3,7-trihydroxy-6-oxo-1,3,5(10),7-tetraene-24-nor-friedelan-29-0ic acid methylester with antibacterial activity against Bacillus cereus, Staphylococcus epidermidis and Micrococcus luteus) from the roots of Crossopetalum gaumerii.

7. CONCLUSION

While it is generally assumed that the use of medicinal plants used in indigenous cultures has a rational basis and that the plants have beneficial health effects, little empirical evidence is available which corroborates this idea. Our investigations show that the indigenous groups we worked with have well defined concepts about plants and that several of the species used by them possess interesting pharmacological effects. While in some instances it was possible to identify a class of compounds, which seem to be responsible for the effects observed, in other cases, for example Hiptis verticillata and Baccharis conferta, several classes of natural products contribute to the pharmacological effects documented.

Taken together these studies demonstrate that the study of indigenous medicinal plants should not be reduced to the search for new molecules or to the use of such plants as potential industrial raw material. Ethnobotany not only contributes to a better understanding of indigenous cultures but - if appropriate forms of returning the scientific knowledge to the indigenous communities can be developed- will also allow these cultures to make improved use of their medico-botanical resources.

Cultures constantly change and in recent decades the rate of change has accelerated drastically. We noticed that these traditions are no longer used by all members of the ethnic groups, and with the loss of native traditions including the native language, the future use of medicinal plants by the the Mexican Indian groups we work with as well as its cognitive base is bound to change drastically. Therefore, we hope that these study also serve as a repository of knowledge and that these studies document which cultures are the keepers of this knowledge. These persons are the original keepers of medicinal plants. These persons are the original keepers of the ethnobotanical knowledge presented here. I am very grateful to all former PhD students in Freiburg and to Prof. Rimpler. The data discussed in this paper are part of the PhD theses of Drs. P. Bork, F. Geiss, M. Hoer, M. Kuhnt, C. Weimann and the M.Sc. thesis of Inga Koehler as well as of the research of Dr. E. Scholz. I am also very grateful to Drs. A. Ankli, B. Frei, M. Leonti and Prof. O. Sticher (all Zurich, CH) for many years of fruitful collaboration on ethnobotany and phytochemistry. In this overview I relied on all their research and in the area of ethnobotany especially on the work of Anita Ankli and Marco Leonti. The research on plant-derived NF-κB-inhibitors would not have been possible without Prof. M.L. Schmitz, Dr. Bacher and their team in Heidelberg (D, now Bern, CH). I am also grateful to Prof. Carlos Viesca Treviño (México, D.F.) for many years of continuous friendship and support as well as to Drs. Jorg Heilmann (Zürich, CH), Heike Vibrans (Texcoco, MX), Andrea Pieroni and Paul Brenner (both London, UK) as well as John Brett (Denver, USA) for interesting discussions and advice. The botanical identification was performed at the Herbario Nacional de México (MEXU) and also at the Herbarium of the Instituto de Ecología (XAL) in Xalapa, Veracruz, the Colegio de Postgraduados en Ciencias Agrícolas, 56230 Montecillo and the Centro de Investigaciones Científicas de Yucatán (CICY), Mérida.

ACKNOWLEDGEMENTS

The ethnobotanical part of this research would not have been possible without the help of many people in Mexico, especially the midwives, healers, and specialists in medicinal plants. These persons are the original keepers of the ethnobotanical knowledge presented here.

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