

What is “traditional use” evidence?

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Abstract

In the age of evidence-based medicine it has become clear that with regard to efficacy the levels of evidence for medicinal products of well-established use and traditional medicinal products are rather different. In the former, evidence is based on bibliographic data and increasingly on product-specific clinical trials. In traditional medicinal products evidence of the efficacy and safety often relies on drug monographs, expert opinions and historical sources. This “traditional use” evidence is the result of a process of trial and error in pre-scientific medicine, which often covered centuries and, by compilation of data, generated the broad spectrum of indications of many traditional medicinal herbal drugs and products. By transferring “traditional” indications into those of “main-stream” medicine during the process of licensing, precious traditional experiences and useful information can be lost irreversibly. This especially applies to combinations of herbal drugs. The new indications of traditional medicinal products include prevention of health problems, reduced states of health of complete organ systems, and adjuvant use in so-called minor indications. This process possibly prevents any further scientific evaluation of the traditional medicinal products by clinical trials, as they usually are planned for clear-cut modern indications. Hopefully, the pre-scientific use of herbal medical drugs is still an important starting-point for modern pharmacological research, as it is well-known that many symptoms and diseases patients suffer from,

still cannot be explained and/or treated by modern scientific medicine. Traditional medicinal products may bear a healing potential that should not be lost.

Key words: well-established use, evidence based medicine, traditional use evidence, herbal medicinal drugs, herbal medicinal products, dyspeptic syndrome, garlic

Introduction

The process of product licensing in the European Union is determined by product-specific evidence of quality, safety and efficacy. This also applies to herbal medicinal products, which however, rather often cannot rely on product-specific randomised clinical trials. In the CD 1999/83/EEC additionally other sources of evidence such as post-marketing studies and epidemiological studies with similar products (bibliographic application) are allowed as a valid proof of safety and efficacy, i.e. “well-established use”. In terms of evidence-based medicine well-established use means evidence level I-III (table 1).

In contrast, the precise definitions of traditional medicinal drugs and products and especially of the traditional use evidence are still intensely discussed. In the following article some criteria are presented which may alleviate the evaluation of traditional use evidence of a medicinal drug and perhaps also of a product and are discussed with the focus on the peculiarities of herbal medicine.

Level of evidence	Methods
Ia	- meta-analysis, several randomised controlled clinical trials
Ib	- at least one randomised clinical trial
II	- at least one non-randomised clinical trial with a well-designed protocol
III	- non-experimental descriptive clinical trials with a well-designed protocol, case-control studies, cohort studies
IV	- not evidence-based expert opinion, monograph, consensus conference etc.

Table 1: Levels of evidence (adapted from (5))

Due to the intense scientific effort in the last 15 years many medicinal herbal drugs/products have been upgraded with regard to their evidence level. For example, peppermint oil as a retarded preparation for treatment of irritable bowel syndrome has reached level Ib, St John's wort (*hyperici herba*) has even reached level Ia (17,18). Many other drugs e.g. herb and root of dandelion (*Taraxaci radix cum herba*) or lesser galangal root (*Galangae rhizoma*), both used for treatment of dyspeptic syndrome, or herb of white dead nettle (*Lamii albi herba*), which is traditionally given for respiratory problems, have remained at evidence level IV (3). These statements seem to be very clear, but many problems show up when one goes into detail.

Garlic, a herbal medicinal drug with several levels of evidence

For further analysis of these problems, a very popular herbal medicinal drug is used. Firstly the problem of indication will be illustrated. The potency of garlic (*Allium sativum*) has been acknowledged for more than 5000 years. In ancient times, the Egyptians, Babylonians, Phoenicians, Vikings, Greek, Romans, Chinese and Indians took garlic as a remedy for intestinal problems, invagination, flatulence, respiratory infections, skin disease, wounds and problems in the ageing process. In the year 77, the military physician Pedanios Dioskurides published the famous *Materia medica* and mentioned garlic cloves or juice as a remedy against flatulence and cestodiasis and for improvement of miction. In other historical sources garlic is recommended for

improvement of the stage of consciousness and of gastrointestinal function (3). In a booklet for health workers in South East Asia from 1990 the WHO states that oral application of garlic as a paste or juice is useful in abdominal gas formation, painful menstruation, abdominal pain and externally oil with juice can be used for pain of the ears (20).

Garlic has been studied extensively, and in more than 3000 publications from all over the world the traditionally recognised health benefits have been confirmed. The active principles in garlic clove are presumably sulfur-containing compounds which have not been fully characterised so far (1). Due to this scientific interest the evidence level of garlic as a herb meanwhile has increased to I for the following indications: adjuvant in hyperlipidemia, and for prevention of age-dependent arteriosclerosis (10). In the ESCOP monograph from 1997 several randomised clinical trials are cited, which support the following indications: Prophylaxis of atherosclerosis, treatment of elevated blood lipid levels insufficiently influenced by diet, improvement of the circulation in peripheral arterial vascular disease, upper respiratory tract infections and catarrhal conditions (8). Garlic clove thereby meets the requirements for well-established use with regard to these indications. In the other indications, randomised clinical studies have not been performed, therefore garlic reaches only evidence level IV, i.e. traditional use evidence. Dependent on the indication the same drug can therefore reach different levels of evidence.

Further problems are dose, preparation and method

of application. In the German monograph, 4 g of intact garlic or equivalent preparations are recommended. This dose has not been substantiated by a scientific reference, only by experience (10). The preparations used include dehydrated powder from raw or dried bulbs or cloves, distillates, extracts and oil macerates. They show enormous phytochemical differences and thereby different effects. Oil macerates for example, have no lipid-lowering effect (4), whereas freshly sliced garlic cloves when applied directly to wounds, inhibit the spread of infections (7). In the ESCOP monograph the equivalent of 6-10 mg alliin daily, typically contained in one clove of garlic or in 0.5-1.0 g of dried garlic powder or other preparations is recommended for prophylaxis of atherosclerosis, while in upper respiratory tract infections 2-4 g of dried bulb or 2-4 ml of tincture (1:5, 45% ethanol) should be applied three times daily (8).

So far, only the drug itself and the preparations for oral application with a daily dose comparable to the monograph's recommendations come up to well-established use, provided that efficacy has been proven by randomised clinical trials. With regard to the different preparations and their corresponding medicinal herbal products, it is sometimes rather difficult to decide whether a definite product can be considered to meet all requirements for the well-established use status. On the other hand, for minor indications, a lower grade of evidence seems to be acceptable. This, of course, is applicable not only to garlic but to all medicinal herbal drugs.

This example demonstrates the difficulty of the decision over whether a herbal drug belongs to the well-established use or to the traditional use department. Furthermore, it also underlines quite well that traditional use evidence presumably has several levels, all of which being the result of mainly direct observations. To be applicable, they should be substantiated, documented, repeatable and suitable for communication. Also, the variability of the observation should be described (23).

The problems of efficacy

Before possible items of traditional use evidence will be proposed, some statements regarding "efficacy" should be made. It is a scientific consensus that effects on the genetic, molecular or cellular level and pharmacological effects in animal models and in healthy humans are not sufficient to prove the efficacy of a drug or a medicinal product. Efficacy can only be proven in patients. Therefore, if this consensus is accepted, only observations in patients should be used as a base for evaluation of traditional use evidence. In reality this is often rather complicated as efficacy has a complex meaning covering improvement, healing or prophylaxis of a disease or improving the stage of consciousness and avoiding complications. Efficacy is the summary of the concrete pretension in the healing process. Presently, in clinical trials, efficacy is measured preferably by so-called hard endpoints such as mortality or hospitalisation. Unfortunately in many chronic diseases these endpoints are not very useful, or even severely biased as a consequence of standardisation. This applies even more to prevention or rehabilitation.

In clinical trials, direct, often monocausal interactions are tested, e.g. clear and measurable effects in a well-defined disease. Therefore the spectrum of diseases investigated is overwhelmingly restricted to those of acute medicine and to acute events in chronically ill patients. In many diseases fulfilling these conditions, clinical trials with evidence level I-III are available, and the safety is well documented. The majority of these clinical trials have been sponsored by institutions and providers with financial interests. These are obliged to control the quality of their products, which also usually underlie a regular control by independent public institutions. Therapeutic progress in this field therefore is more or less the result of primarily financial interests. Physicians and other therapists have mainly undertaken the role of qualified distributors who are obliged to keep up with new developments, to revise them critically and to fit them into the concept of treatment. This is nowadays often done by generation or adaptation of a guideline. The

abundant number of already existing guidelines, which are sometimes contradictory, illustrates the problems of this process. In these guidelines, very often treatment with evidence level IV is not even mentioned.

In the abundant part of medicine including e.g. surgery, internal medicine with the exception of acute diseases or diseases which can be classified easily, psychotherapy, psychiatry, neurology, prevention, rehabilitation, and metaphylaxis of chronic diseases, clinical trials in the sense of evidence-based medicine are often difficult to perform. Treatment therefore relies predominantly on experience and observations documented by monographs, textbooks, expert opinions, consensus conferences and historical sources, which means evidence level IV and includes both efficacy and safety. The quality of treatment often depends on the physician or other therapists, in surgery increasingly from the use of robots, and in prevention and rehabilitation from an individualised treatment concept which may consist of several modules. Research is mainly sponsored by governmental institutions, health organisations, foundations and other independent institutions and of course by the producers of technical devices. The results of this research often is not even mentioned in medicinal guidelines.

Traditional use evidence of medicinal herbal drugs and products is clearly part of evidence level IV or even below. Controlled clinical trials are not available, as these drugs are not interesting with regard to financial aspects or because they are used for minor indications or in self-medication for which a lower grade of evidence seems to be acceptable. Clinical trials with these indications are often difficult to perform for statistical and other reasons. Therefore the majority of these drugs and medicinal products presumably will stay in category IV forever. The underlying problem is the conflict between their drug status, which makes them subject to all legal control mechanisms for medicinal products, and their traditional use. If in the long term the control mechanisms would be the winners in this conflict,

these drugs and products may lose their medicinal drug status. Then, valuable traditional knowledge and experience may be lost for ever.

Items determining levels of traditional use

The traditional use evidence of one definite herbal medicinal drug can be very different from the other. For example, the drug “herb of white dead nettle” (*Lamii albi herba*) is used traditionally for respiratory problems according to expert opinion and historical sources, whereas a positive German commission E monograph exists for the external (traditional) use of the leaves of walnut-tree (*Juglandis folium*) (3,13). This example already shows up the possibility of the existence of several levels within traditional use evidence. For classification, several items which are shown below can be used.

The type of documentation of traditional use is clearly very important. Generally, monographs are accepted as superior to results of consensus conferences, recommendations in textbooks, expert opinions or historical sources, the evidence level supposedly declining in the order of mentioning. Monographs should only be considered to be part of evidence level IV when they are not based on adequate clinical trials. A typical example is the German drug monograph for bitter orange peel (*Aurantii pericarpium*)(11). This drug and its use is also mentioned in modern textbooks on phytotherapy (17,21) and in several historical sources (3). In the German monograph, the drug is recommended for the indications anorexia and dyspeptic syndrome, in historic sources the drug is used as an appetizer and digestant. This remarkable consistency within the historical and present day use is also a strong indicator of a high level of traditional use evidence.

The geographical distribution of the use of a herbal medicinal drug can be a further item to determine its traditional use evidence. If the use is documented world-wide, this means a higher classification than a use within a continent, in several countries, in one country or only regionally. Of course one also has to consider the geographic availability of the drug. Clove

(Caryophylli flos) is traditionally used in south-east Asia, where it is cultivated, but also in Europe, to stimulate digestive function and to strengthen the mucosa of the oropharynx (3) and for treatment of coughs and toothache (20). The wide distribution of this drug for centuries was supported by its low weight and stability.

Temporal aspects can also be used for classification of traditional use evidence. Some herbal medicinal drugs such as onion (*allii cepae bulbus*) have been documented since Egyptian times, the laxative and diuretic effects of figs (*Caricae fructus*) have been described by Dioskurides (77 p.C.), cloves (*Caryophylli flos*) have been known to mitigate toothache since the description by Ibn al Baitar, who died about 1250 p.C., while the use of the bark of condurango (*Condurango cortex*) for treatment of gastric ulcer has been mentioned only in 1877 in a German textbook (3). The use of Siberian ginseng (*Eleutherococci senticosi rhizoma*) is documented in a German textbook only in 1975 (3). These examples illustrate that the temporal aspect of the traditional use of a drug is by no means sufficient for the classification, as the knowledge of the healing potential of drugs derived from non-European plants is very often much older, at least in the respective countries of their origin. Therefore, it is worthwhile in many cases to investigate the history of the use of a herbal medicinal drug not only in European documents.

This leads to the next item, the type of documentation. For millennia, copying of manuscripts has been the only method besides oral tradition, to keep precious knowledge for the following generations. Many famous ancient books were copied literally in the early and medieval Christian monasteries, thereby preserving knowledge from the antiquity. The *Materia medica* by Dioskurides was a main source of the phytotherapeutic knowledge in Europe until 1800 (3). In terms of classification of a traditionally used drug, documentation in many independent sources seems to be superior to only a few independent documents, even less valuable are many

documents which rely on few sources, or many documents or even only one document which rely on one source. There may sometimes be documents without any sources, this of course should raise some suspicion.

Traditional herbal drugs are often applied in a traditional form of application such as tea, tincture, juice or syrup. Modern forms include often rather precisely defined extracts or special extracts in e.g. pills or capsules. Only a stable form of application used for at least three decades, perhaps including minor alterations seems to be compatible with traditional use.

The indications for the traditional use of a medicinal herbal drug are sometimes very stable, sometimes they change over the course of time. A stable indication may have been used since ancient times, for a millennium, for centuries, decades, or only a few years. Indications may have been adapted according to new findings in medicine or even completely changed if an indication had become irrational. For example one of the indications for caraway in the *Materia medica* by Dioskurides was for the improvement of digestion, and even nowadays it is used for that (3). On the other hand, in China the fruit of the ginkgo tree (*Ginkgo biloba*) was traditionally used in asthma bronchiale, nowadays the indications for the extract from ginkgo leaves are vertigo, tinnitus, intermittant claudication, and dementia (3,12). This is also a good example of the complete change of the use of a medicinal plant. The traditional use according to a special medicinal or philosophical background, e.g. therapy according to the individual constitution, will be dealt with below.

There are often problems with regard to consistency in the description of the name or the species of a medicinal plant or a medicinal herbal drug. This can be due to various reasons such as wrong translation from a foreign language or a dialect, or incorrect copying from old manuscripts. Examples are camomile (*Matricariae flos*), which cannot be precisely identified in the *Materia medica*, but has

been described by Hieronymus Bock (1489-1554) (3). A recent example is the confusion of *Echinaceae pallidae radix* with *Echinaceae angustifoliae radix* and vice versa, which happened frequently until 1990 (2). A possible classification may be a persistence with regard to description, name and/or species for at least three decades, with minor or major alterations or a complete change in the decades or centuries before. Changes in the recent three decades should result in a loss of the traditional status.

This scheme can be applied very similarly to a drug and/or its preparations used: No change for at least three decades, with minor or major alterations or a complete change in the decades or centuries before. This may raise some problems in herbal medicinal products. For example, in response to the requirements of the changes in the German drug law, the number of constituents of herbal medicinal products has often been reduced in the last ten years. Therefore, the rules for the claim to be traditional may differ between herbal medicinal drugs and their products.

Indeed, traditional use in herbal drug combinations or the respective medicinal products seems to be a special and very complicated issue. The most important question is whether a combination of herbal drugs can be looked at as a whole or as a composition of several herbal drugs. Both views have their advantages and disadvantages. The view of a herbal combination as a whole seems to be easier, as all items listed above can be applied in the same way as long as the components have not been changed at all for a certain period of time. In the European Commission's "Directive on Traditional Medicinal Products" this period is proposed to be three decades (6). Presumably this holds true for only few herbal medicinal products, as many were changed according to legal processes or in order to improve the products according to modern scientific knowledge. It would be more than unfair to blame the products for these changes.

The view that a herbal medicinal drug combination

product is a combination of herbal drugs, which one by the other have to be examined, whether and how traditional they are according to the items proposed above, raises many problems, for example, which of the components is(are) the most important one(s) or which determine(s) the traditional use evidence. Is it the main component or the component which may be the most effective one (this may be interesting for example in a bitter) or that with the longest traditional use? Can the problem possibly be solved by creating an index? There are still many problems to be dealt with.

Problems of diagnosis and indication

Traditional use of herbal medicinal drugs does not only mean that they are used traditionally, but also the purpose of the use of a herbal medicinal drug may be a "traditional" one. Medicinal drugs, especially the herbal ones, are used for indications. For example, marshmallow root (*Althaeae radix*) can be efficaciously applied for the indications dry cough and irritations of the oral, pharyngeal or gastric mucosa (9). These symptoms can occur in many diseases.

Due to the intense activities in medical research, the etiologies of many diseases have been identified in the last 15 years, and their pathogenesis and symptoms are more precisely defined than ever before. This development allows earlier and more precise diagnoses, and hopefully, a more efficient treatment, but it also caused an increasing problem, which is often not realised and can be paraphrased with a discrepancy between diagnosis and indication. A patient who suffers from the symptoms of a disease does not care for this theoretical problem as he primarily wants to be free from the symptoms and, if possible, to be cured. The modern physician, who is obliged to work on a scientific base as far as possible, prefers to derive the adequate treatment from a precise diagnosis. Diagnosis means the nosological-systematic denomination of a disease. From the practical point of view it is the sum of findings from diagnostic measures. Indication is by far more patient-orientated and means the reason(s) for applying

adequate medical treatment, which after assessing possible advantages and risks - and paying attention to possible contraindications - is useful for the patient. Currently, mainstream medicine is dominated by treatment of diagnoses, not by treatment of symptoms, and this trend will presumably be stable. Some serious problems of diagnosis-orientated medicine are - reduced compliance, as patients are often not willing to be treated whilst not suffering from symptoms, and high costs, because many diseases can and should be treated already in a symptom-free stage.

The present problem of acceptance of medicinal herbal drugs is an excellent example of the discrepancy between diagnosis and indication. Most herbal drugs are applied in more or less traditional indications as for example dyspeptic syndrome or diarrhea, only some drugs are used in patients with a rather defined diagnosis. A representative example is butterburr (*Petasitidis rhizoma*), which is applied as an adjuvant to treat acute colic of the lower urinary passages and is traditionally used in dyspepsia, to induce sweating, and externally, for moist wounds (3, 15). In recent clinical trials it has been shown to be helpful in migraine. Migraine is an example of a symptomatic disease with a long tradition, which is nowadays much more precisely defined, but still has the old label. Many new diagnoses have been established which have completely replaced older ones such as dropsy, some diagnoses have even been abandoned completely in modern medicine, such as the constitutional ones which are based on the imagination of an imbalance in the vital energy of the patient. Some centuries ago in Europe, treatment had two purposes: a) to relieve symptoms and b) to rebalance vital energy. For example, radish (*Raphani sativi radix*) was used as a digestant, but also, as it is "hot" in the sense of constitutional medicine, to increase energy in the gastrointestinal tract according to the constitutional diagnosis (3).

Of course, symptoms are present irrespective of the philosophy of the underlying medicinal system, and medicinal drugs are used for their relief, with or without a precise diagnosis. It is regrettable that

indications are not very often the subject of recommendations and systematic reviews in evidence-based medicine and of clinical trials. Also, refunding of the costs by the health insurance system becomes increasingly dependent on a standardised diagnostic procedure leading hopefully to precise diagnosis, preferably an ICD-10 based diagnosis. Therefore research and treatment with herbal medicinal drugs may be more difficult in the future than it has been in the past, especially for traditionally used drugs. For example, the dried fruit of bilberry (*Myrtilli fructus*) is traditionally used, without any doubt with regard to its efficacy for the indications - acute unspecific diarrhea and mild oral and pharyngeal mucositis due to various diseases (diagnoses) especially in children (14). There is no medicinal herbal product on the German market so the drug itself has to be prescribed. In the case of planning a clinical trial with bilberry fruit, one has to decide whether the indication(s) or a disease causing the symptoms should be tested. Sponsoring is presumably hardly available. If choosing one of the indications it may be difficult to publish the results in a peer-reviewed paper. The only possible way to preserve this well-tolerated herbal medicinal drug for the future may be self-medication.

The treatment of dyspeptic syndrome by medicinal herbal drugs

In order to illustrate the various difficulties in traditional use of herbal medicinal drugs and products, an example may be set. In Europe, more than 65 herbal medicinal drugs and various combinations are traditionally used for treatment of dyspeptic syndrome (3). Combinations of drugs seem to be more efficacious, but attention should be paid to a sufficient concentration of the effective constituents, which means that combinations with more than a few ingredients are not very efficacious. The herbal drugs can be applied a) according to the supposed individual pathomechanism(s) of the syndrome representing the biomedical approach, b) according to the individual symptoms which stands for the conventional treatment, or c) according to the individual constitution type, which is the traditional or historical

concept. By the way, the diagnosis “dyspeptic syndrome” cannot be found in the list of the International Classification of Diseases (ICD-10).

The herbal drugs can be classified according to the effective constituents. Some examples are mentioned.

- Aromatics/essential oils: Anise (*Anisi fructus*), fennel (*Foeniculi fructus et aetheroleum*)
- Alkaloid drugs: Fumitory (*Fumariae herba*), celandine (*Chelidonii herba*)
- Flavonoid drugs: Bitter orange (*Aurantii pericarpium*), German chamomile (*Matricariae flos*), milk thistle (*Cardui mariae fructus*)
- Drugs with mustard oil glycosides: Black radish (*Rhaphani sativi rhizoma*).

The method of action of the constituents is well-known. Essential oils increase the secretion of gastric juice, increase the motility of the stomach and intestines, relax smooth muscle cells of the intestines and increase absorption of flatulent gas. Alkaloid drugs inhibit the effect of acetylcholine, thereby reducing intestinal spasms. Flavonoid drugs have a lot of different drug-specific effects: they are spasmolytic, reduce the permeability of capillaries, stabilise cell membranes, are antihepatotoxic, antiinflammatory and/or antioxidative. Drugs with mustard oil glycosides are mild laxatives, antibiotics and cholekinetics, they increase motility of the intestines. If the gastrointestinal dysfunction can be specified exactly, herbal medicinal drugs can be applied according to the biomedical approach. In reality, this is very often not possible due to the unknown aetiology and pathogenesis of dyspeptic syndrome.

The drugs can also be classified with regard to their effect(s):

- Adstringents: Greek sage (*Salviae folium*)
- Amara: Artichoke (*Cynarae folium*), dandelion (*Taraxaci radix cum herba*)
- Amara/aromatica: Calamus (*Calami rhizoma*), hops (*Lupuli strobulus*)
- Antidiarrhoics: Bilberry (*Myrtilli fructus*)
- Carminatives: Calamus (*Calami rhizoma*)

- Cholagogues: Cardamom (*Cardamomi fructus*)
- Cholekinetics: Peppermint (*Menthae piperitae folium et aetheroleum*), lesser galanga (*Galangae rhizoma*), wormwood (*Absinthii herba*)
- Choleric: Horehound (*Marrubii herba*)
- Laxatives: Buckthorn (*Frangulae cortex*)
- Mucilaginoso: Flax (*Lini semen*)
- Spasmolytics: German chamomile (*Matricariae flos*), celandine (*Chelidonii herba*).

This classification relies mainly on the symptoms of the patient and tries to counteract the supposed pathological processes of the more or less descriptive diagnosis. For example a patient with painful flatulence and abdominal spasms will profit from spasmolytic and carminative drugs.

A further classification can be made with regard to sensorial aspects.

- Bitters: Yellow gentian (*Gentianae radix*), condurango (*Condurango cortex*), dandelion (*Taraxaci radix cum herba*)
- Pungents: Ginger (*Zingiberis rhizoma*)
- Drugs with essential oils: Coriander (*Coriandri fructus*), lavender (*Lavandulae flos*)
- Spices: Coriander (*Coriandri fructus*), caraway (*Carvi fructus*).

This classification is used for the traditional constitutional treatment. For example, pungents and essential oils are claimed to be hot and energising, the so-called tonics. They are used “to strengthen the stomach” in patients who have pain in the stomach region, cramps and stomach noises 2-6 hours after eating and they also improve the general condition of these patients who often feel weak and tired. In clinical studies using these drugs according to their chemical components, effects have been shown that are compatible with the new as well as the old description of pathogenesis of the disease/symptoms (22). Therefore, with regard to traditional use evidence, at least sometimes the evidence level of a traditionally used herbal medicinal drug or product could be increased by clinical trials without the risk of forgetting the traditional indication and knowledge.

Traditional use evidence – tasks for the future

Traditional use evidence can be defined with regard to several points of view: The medicinal herbal drug/product itself, the modern or traditional diagnosis, the indication (symptom- or disease-oriented) and the medicinal system (traditional or modern mainstream). In order to prevent the loss of precious knowledge, collecting material by using all sources available is the first step to be done. This is a national, but also an international task which includes in a second step, comparisons of subspecies, and pharmaceutical, pharmacological and clinical aspects. In a third step, evaluation of drug potential by pharmacological tests may follow and clinical trials. Especially the developing countries will become important partners as they have a basic interest in traditional medicine due to their difficult financial situation. Further tasks are the careful conversion of traditional indications to modern ones and the testing of new indications for herbal medicinal drugs in clinical trials. Last but not least, therapists and patients must be informed precisely and independently to improve the level of self-medication.

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