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Standardisation of herbal medicines – the natural way, illustrated by the example of fresh plant preparations

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1. Introduction

Why is the demand for herbal medicines so great in the modern technological world? We humans have not only technical and scientific part in us but also an intuitive and instinctive part. Plants can resonate with our instinctive nature. A flowering alpine meadow, for example, shows us the multitude of different plants growing together in a natural balance. Because we also possess an intuitive part in us, it is not difficult for us to find joy in these plants. They have developed alongside us through all stages of evolution. There is thus a particular relationship with many plants, based on an extremely valuable traditional knowledge of their actions as medicinal herbs.

How can we now manufacture standardised herbal medicines and thereby bring our scientific and instinctive parts together?

First of all, we should not disturb the natural constitution of plants, i.e. the varied composition of plant constituents. In this respect we must recognise that we still know almost nothing about the constituents, their interactions and their very complex mechanisms of action in our body. We do not know how a plant extract with its thousands of constituents acts, or how the various constituents influence each other during absorption and "docking" with hundreds of receptors. We should therefore be cautious about qualifying certain groups of constituents as inactive or ballast. Even during cultivation it is possible to distort the natural constitution of plants, e.g. by the use of herbicides, fungicides or artificial fertilisers (Denke et al. 1999). With the modern technological ability to produce genetically modified plants, we even have to consider new plants to which none of the traditional knowledge can be applied.

Of course, we can no longer collect our medicinal plants in the required amounts from alpine meadows. However, knowledge on cultivation of most medicinal plants was gathered over generations. We need to apply scientific methods to process and further develop this knowledge in the sense that the natural constitution of the plant is maintained and our environment is protected.

All these points have been completely ignored in the recent discussion about essential similarity of medicinal plant products that has been motivated exclusively from a technocratic point of view (Kooperation Phytopharmaka 1995; Gaedcke 1995; Zündorf 2000).

In parallel with this is the increasing discussion of the rational principle of standardisation, i.e. the definition of a plant preparation not by the drug/preparation ratio achievable with a given solvent but by a frequently dubious standardisation on individual constituents. Quality based on non-specific assay of individual constituent-groups (e.g. flavonoids) would be adequate if this could describe the mechanism of action. However, the actual active constituent is often unknown and standardisation is based on so-called marker substances. The example of valerian shows the grotesque consequences this approach may have: the changes in content requirements in the different editions of the pharmacopoeia during the last decades depended greatly on the actual state of scientific knowledge, but even today the exact mechanism of action of valerian is still unknown.

It is interesting that the GMP rules that have been internationally valid for many years are being extended through a note for guidance on specifications for

Abstract

All living creatures are influenced by the law of natural variability. In the standardisation of herbal medicines, the uniformity of contents is also affected by this law because the starting material is a natural material. Using the example of herbal medicines prepared from fresh plants, the factors influencing active ingredient contents are demonstrated. The variability of quality parameters depends on the genetic properties of the plants, the ecological conditions during the vegetative period and the manufacturing process. Even under optimal conditions the contents may vary by plus or minus 50%, up to now accepted as tolerable. Registration authorities have recently started to examine drug licence applications for herbal medicines in the same way as chemical drugs and demand similar tolerances. For the natural reasons and from the viewpoint of the medicine it is clear that, as shown by the examples, this is neither possible nor necessary with complex mixtures such as herbal medicines.

Key words

Herbal medicinal products, standardisation, natural variability, uniformity of content, fresh plant products, medicinal plant cultivation.

herbal medicinal products. The question of acceptable analytical variation is quite pragmatically being adjusted to match the natural range of variation.

On the other hand there is a new trend among the European registration authorities to require narrow limits for content specifications in the description of the model quality, analogous to those for chemically defined substances. However, this approach does not make allowance for naturally occurring variations and is technically impossible to apply in daily production.

The following report is intended to show the degree to which the achievable limits of variation are influenced by the natural variability of the plants themselves and by the processes used to manufacture the products. Finally, these parameters are considered also in relation to the desired therapeutic action.

2. Which factors influence the quality of herbal products?

The aim of standardisation is to obtain herbal medicines with consistent efficacy, only ensured if all constituents are present in similar amounts from one dose to another. To achieve this standard the following model has been proved in practice.

The main pillars of standardisation are the *plants* used as raw materials and the product *manufacturing process*. All data and information obtained on the corresponding plant varieties, their cultivation and the product batches obtained are collected, evaluated and applied continuously to improve product quality.

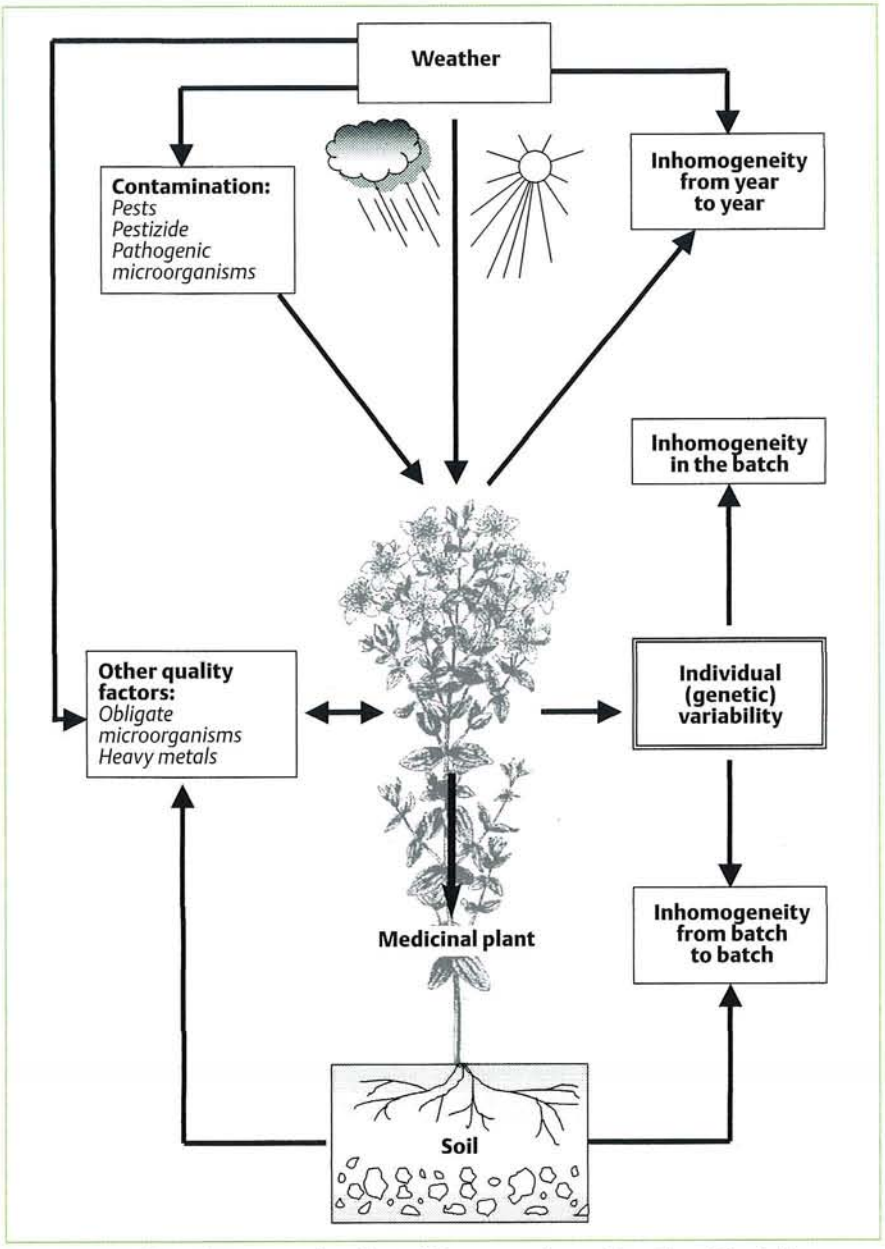
2.1. Plants as raw materials

Like other living organisms, medicinal plants are subject to variability of all features and to the effects of ecological factors and genetic disposition (see **Figure 1**).

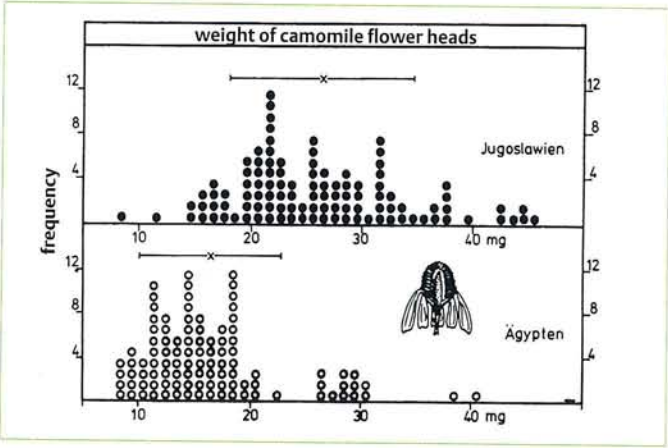
One of the most important methods in biology is thus the detailed observation and characterisation of all individual features, whereby the quantitative consideration of features is particularly important. If the individual values for specific features are considered in a group of living things, it is found that they are grouped in the form of a normal distribution around a mean value; with an ideal gaussian distribution, this is expressed by a belljar curve.

This variability of genetically pure lines of various plants differing from each other in specific features was analysed in the work by the Dane W. JOHANNSEN (1926). These differences are genetically fixed and are thus an element of the genotype. However, for various reasons, such as the position of the parent plants and the resulting variations in the supply of the plant organs with assimilates and other building-blocks, the features are formed differently in each plant. Their distribution, which is governed by external factors, e.g. ecological factors, represents an element of the phenotype, which is determined by interaction of hereditary and environmental factors.

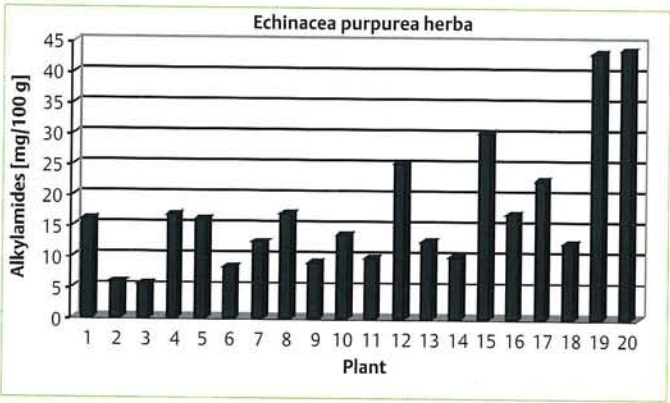
Consequently, apart from the usual diagrams, the principle of normal distribution is illustrated by the use of histograms also. The breadth of this bellcar curve and thus the range of variability of



▲ *Figure 1: Effect of genetic and ecological factors on the quality of medicinal plants.*



◀ *Figure 2: Histogram of the morphological parameter »Size of camomile flower heads«. Two genetically different varieties with clearly different flower sizes are compared.*



◀ *Figure 3: Variations of concentrations of constituents in Echinacea purpurea herbage. Alkylamides content in individual plants from a defined variety, with identical crop site and harvested at the same time.*

the examined parameter depends on the genotype (= influence of genetics) and phenotype (= influence of ecological factors and the physiological parameters dependent on them).

2.1.1. Influence of genetics:

When considering morphological parameters such as the size of camomile flower heads, the genotype principle is obvious since this feature is easily comprehended (**Figure 2**). The same thing is, for example, found in looking at the stature in humans. When large populations are considered, a similar gaussian distribution of the different heights is observed.

However, chemical features such as the formation of secondary plant constituents are also subject to this biological principle.

The variations in constituent concentrations among individuals of a natural plant source are illustrated using the example of Echinacea constituents (**Figure 3**).

The contribution of genetic disposition is particularly clear when considering resistance to pests, especially in studies of various climatically different growing sites.

Figure 4 illustrates the resistance of St. John's Wort *Hypericum perforatum* from various sources to the pathogenic fungus *Colletotrichum gloeosporitoides* causing wilt as an example of a typical genotypic feature.

In the first year, 100 wild types were tested in a greenhouse and 24 proved to be usable as field crops. In the second and third years these 24 varieties were grown in three different crop sites in the Wallis canton (Gaudin 1999). The major selection criterion was propensity to wilt. Only four varieties were tolerant of this ubiquitous fungus in the three sites during both these years.

In any event, the choice of optimal plant varieties is one of the most important contributions to the standardisation and quality of a herbal medicine.

In summary, the list of criteria for optimisation of varieties with regard to the influence of the plant on variability can be compiled for St. John's Wort (Hypericum perforatum) as an example. The following parameters emerge as selection criteria:

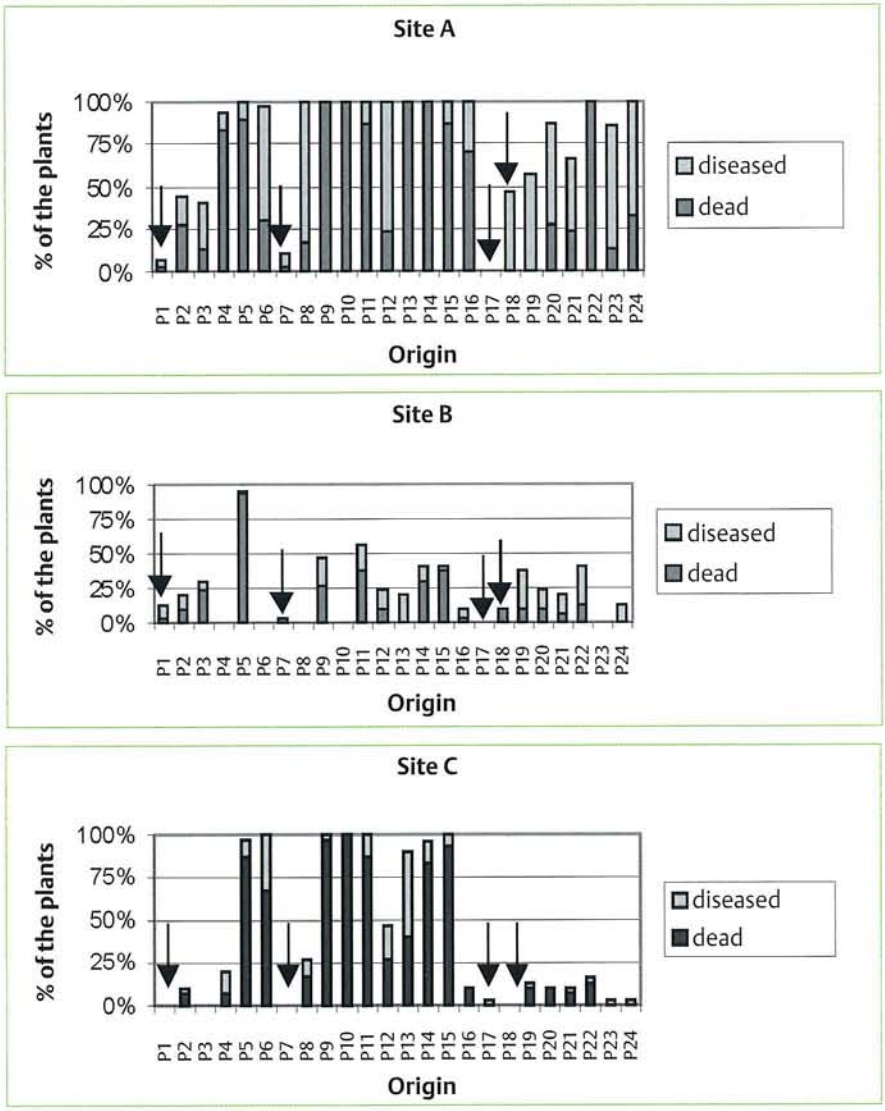
- Susceptibility to wilt (caused by the fungus *Colletotrichum gloeosporitoides*)
- Narrow flower horizont for easy harvesting of the upper flowering shoot tips of 15 cm length, since this part of the plant contains the known constituents in elevated concentration (American Herbal Pharmacopoeia 1997)
- Good crop growth at various sites (different soils, different altitudes, etc.)
- Optimal concentration of pharmacologically active constituents such as hypericins, hyperforins and flavonoids.

2.1.2. Effect of ecological parameters

The genotype, which can be influenced to a certain extent by breeding and selection, is overlayered by far greater variability due the effects of environmental factors. The phenotype can hardly be predicted since climatic conditions cannot be controlled in field-grown crops of medicinal plants. With these crops, therefore, the choice of correct site and optimal time of harvesting are to be seen as critical parameters influencing the constituent pattern and concentration. With other plant products, these phenotypic variations even have become a cult, as in the case of the "science" of vintages of wines from specific growing regions.

The example of *Hypericum* illustrates the problem of the choice of the correct crop site.

The relative concentrations of constituents in St. John's Wort are primarily dependent on variety. Independent of crop site, a good variety always contains higher concentrations than a weak variety (**Figure 5**). The same applies to undesired constituents such as cadmium.



▲ ***Figure 4: Infection of Hypericum varieties with St. John's Wort wilt (% affected plants). Results in autumn 1997 and before harvest in summer 1998 in 24 St. John's Wort varieties at three different sites. The 4 tolerant varieties are marked with arrows.***

However, a variety of good quality need not have agronomic properties that like-wise are suitable for all crop sites. It needs some years of experience with the four selected varieties on a larger scale, to turn out which variety is best for soil and climate types. This already reveals one important natural limit to standardisation. To ensure supplies, crops have to be grown at various sites. If different varieties are used to minimise the risks in controlled growing, this will also increase the natural variability of constituent concentrations in the medicine.

The example of *Echinacea* illustrates the influence of crop site on constituent variability.

The correct crop site and the correct time of harvesting are also determined on the basis of comprehensive analytical data for production batches. Only data for large batches are valid. Usually used data obtained from a few kilograms of a plant from a field trial or even data obtained from single plants can be misleading due to their great variability. **Figure 6** shows the alkylamide variability in large scale production batches of *Echinacea purpurea herba* tincture from various crop sites over several years with the same seed source.

On average basis with regard to alkylamide concentration all eight contract growers supply equally good quality within the usual range of variability.

Constituent variability is also markedly dependent on time of harvest. Therefore it is important to know this optimum time for each medicinal plant and for each of their constituents influencing quality. The best harvest time with regard to the alkylamide concentration of Echinacea herbage is August (**Figure 7**). Since the best time of harvest with regard to cichoric acid is July, the optimal harvest date is given as the period between July and August.

As illustrated just by these examples, it normally takes 5–8 years to get to grips with the plant standardisation factors of optimal variety, best crop sites and correct time of harvest. And the economic consequences of this effort cannot be predicted in any way.

2.2. Manufacturing process:

In parallel with the optimisation of harvested material it is necessary to find a manufacturing process that is suitable for the plant material and does not adversely affect its con-stituents. This procedure is demonstrated in the example of the manufacture of fresh plant preparations.

To compare a manufacturing process in which the optimal plant variety obtained from controlled organic crops is extracted in the fresh state with a normal manufacturing process applied to dried drug material see **figure 8**.

In the manufacture of fresh plant preparations, the plants are extracted immediately after harvest with ethanol at various concentrations so that the native constituents pass directly into the product and are not altered by a drying process of the plant material. There is no storage of the plant material so that disinfestation by fumigation is unnecessary. The restriction to pure ethanol as extraction solvent allows a very gentle evaporation process during dry extract procedure and thus minimal loss of

volatile constituents since very small residues of toxic solvents do not have to be removed in the case of ethanol (unlike other solvents and denaturated alcohol), thus avoiding the need for high temperatures and high vacuum.

Looking at the critical steps of a pharmaceutical production process, some special factors need to be noted in the case of plant preparations. In order to learn all aspects of the manufacturing process for these herbal medicines, experience and results are needed from the product development phase as well as process validations for several production batches covering at least two harvest years. In actual fact, the production process is learned only after several years of production due to natural variation. The production process for an Echinacea tablet serves as an example for this.

The following production steps are critical for the quality of the end product:

- Storage of fresh plants after harvest → must be limited.
- Shredding of the fresh plants → since rapid enzymatic breakdown of cichoric acid oc-curs here so the shredded plants must be placed in ethanol within seconds (**Figure 9**).
- Extraction → an optimal extraction time can limit further cichoric acid breakdown (**Figure 10**).
- Evaporation → alkylamide losses can be avoided by gentle technology.
- Correct blending of extract batches → contribution to standardisation.
- Tablet mixture → correct excipients can restrict oxidation of alkylamides in the tablets.

The following two process steps may be considered as examples.

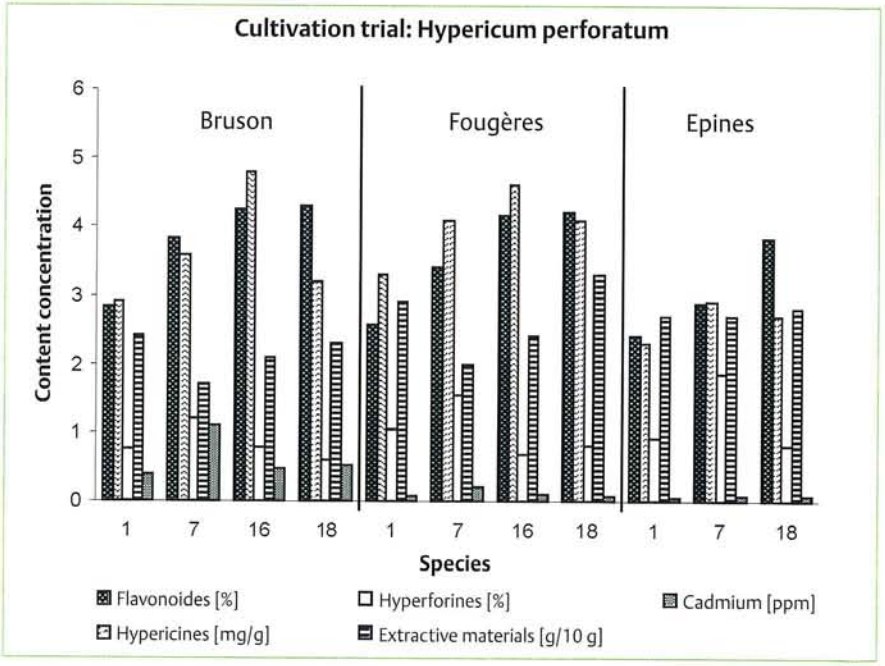
Firstly, the effect of the shredding method on the oxidative processes in the product requires particular attention. **Figure 9** illustrates the effect of shredding time and entry of oxygen on the constituents of *Echinacea* herbage.

In addition, the extraction kinetics of the constituents are decisive for the quality of the end product. The time-dependent extraction behaviour of some constituents of fresh *Echinacea* herbage in the stated extraction process is shown in **Figure 10**.

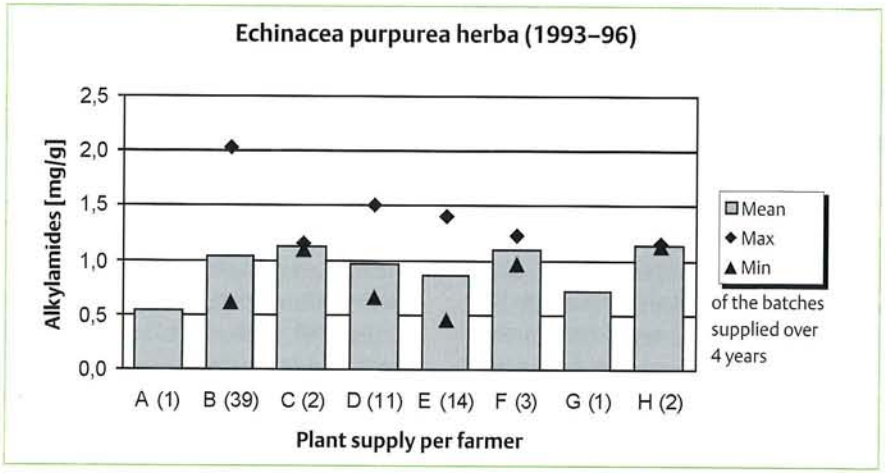
By careful monitoring of production according to the development data and by validation of critical parameters, the

Box 1: Data for the 3 St. John's Wort crop sites in Switzerland (Wallis canton):

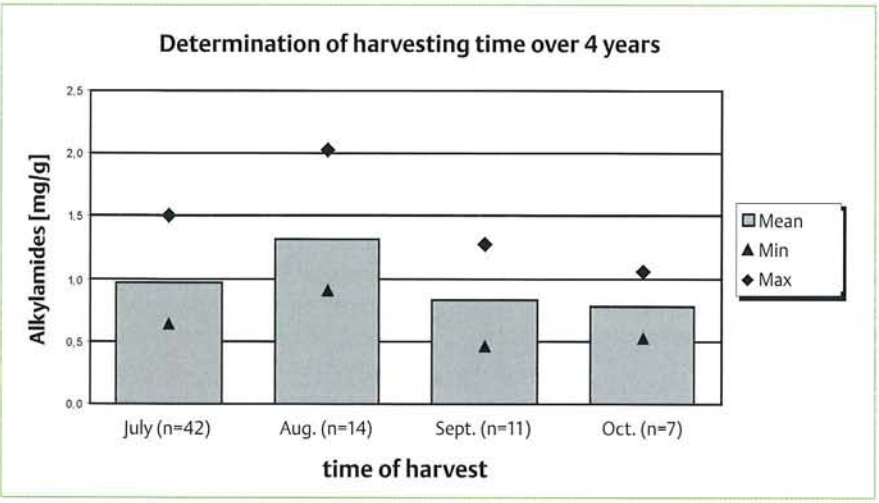
	Epines Site A	Bruson Site B	Fougères Site C
Altitude (m)	480	1060	480
Soil	sandy pH 7.9	sandy loam pH 6.8	loamy pH 8



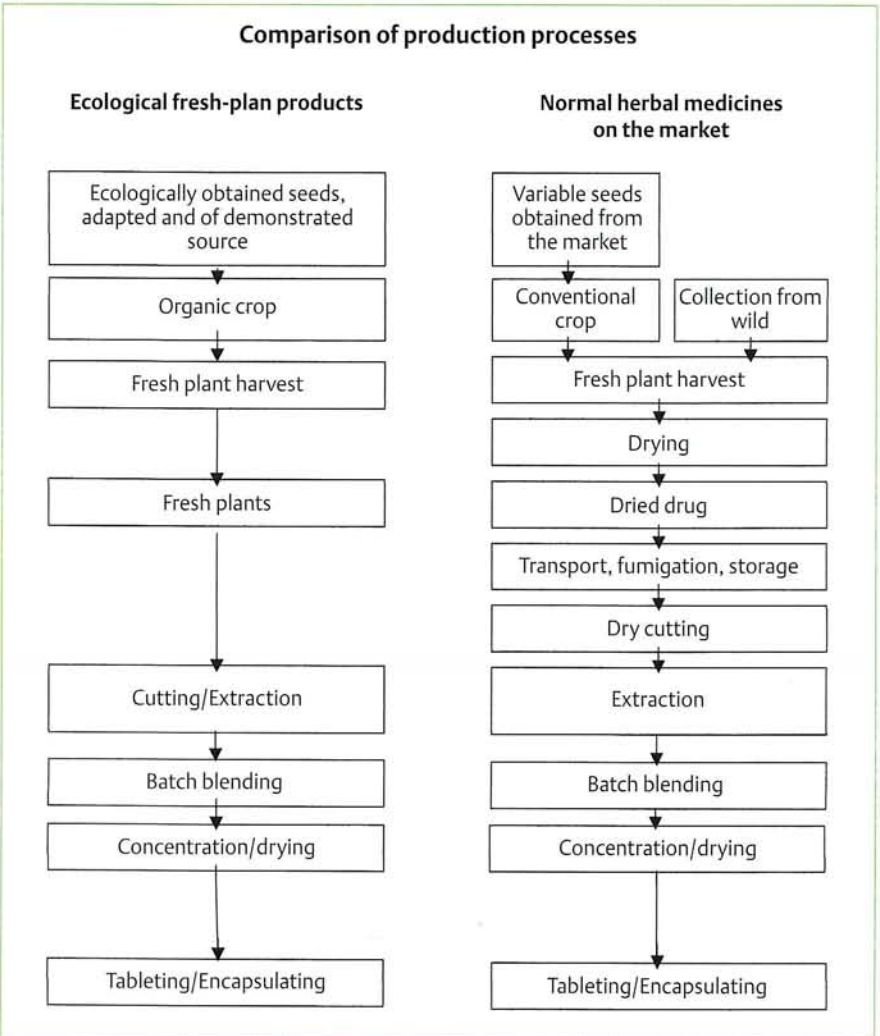
▲ ***Figure 5: Choice of correct crop site, illustrated by the example of Hypericum. In a comparison of 4 selected varieties it is clear that a good variety always has a higher constituent concentration than weak varieties, irrespective of site.***



▲ ***Figure 6: Effect of crop site on constituent variations, illustrated by the example of Echinacea. Example: 39 production batches of Echinacea purpurea herba delivered from one crop site (supplier B) between 1993 and 1996 were processed to tinctures and their alkylamide contents (relative to the amount of dried plant material) were determined.***



▲ *Figure 7: Effect of harvest month on the alkylamide content of Echinacea purpurea herba. Production batches of tincture (1993–1996) were analysed and the alkylamide content (relative to the amount of dried plant material) was calculated.*



▲ *Figure 8: Comparison between the production of ecological fresh plant products and classical herbal medicines.*

technologically governed variations can very easily be kept small, although the plant properties described above also affect the technical process results.

3. How can the variability be reduced?

The starting point for most herbal medicines of the market is usually a raw material composed of medicinal plants collected in the wild and in which the variability of quality parameters must be maximal due to the higher variability of genetic and ecological influences. By growing defined source plants or varieties, the genetic variability is controlled to some extent and the environmental effect can at least be predicted by measurements.

With regard to manufacture, an additional, if not great, reduction of variability can be obtained by the use of validated methods and strict maintenance of manufacturing parameters.

Further optimisation is obtained, in so far as is possible, by blending various batches from a year's campaign.

This is illustrated by comparing the quality data for various batches of *Hypericum* (**Figures 11a + b**) and *Echinacea* (**Figures 12 a + b**). The altered normal distribution and the reduction of variability between the individual batches and blended batches are clearly shown.

4. What variations have to be considered?

What degree of standardisation of a herbal medicine can be achieved by accurate recognition of the two standardisation pillars of "plants" and "manufacturing process"?

The following table with data evaluated on the basis of many years of experience in the determination of constituent groups in various herbal medicines gives a summary of the variability encountered and its reduction by the measures discussed above.

The cases shown in the table can be illustrated by comparing examples of batches of *Hypericum* and *Echinacea* from various sources.

- Regarding point a) of the box 2: 100 production batches of wild-collected St. John's Wort were analysed over 5 years. The content variations were smoothed by blending 20 individual batches per year to provide yearly blends (**Box 3**).

- Regarding point b) of the box 2: Evaluation of 16 production batches of *Hypericum* extract over 2 years, produced from controlled St. John's Wort crops (**Figure 11 a**), and of 62 production batches of *Echinacea* tincture over 4 years (**Figure 12 a**). *This measure leads to a marked reduction of variability.*

- Regarding point c) of the table: When the individual batches obtained from crop plants were additionally pooled to give yearly batches there was a further reduction of variability. As examples, Hypericum blends are illustrated in **Figure 11 b** and Echinacea blends in **Figure 12 b**.

The variability will tremendously increase by comparing a cross section of herbal medicinal products from the European market due to variation of raw material but also by differences in manufacturing processes and different definitions of the preparations.

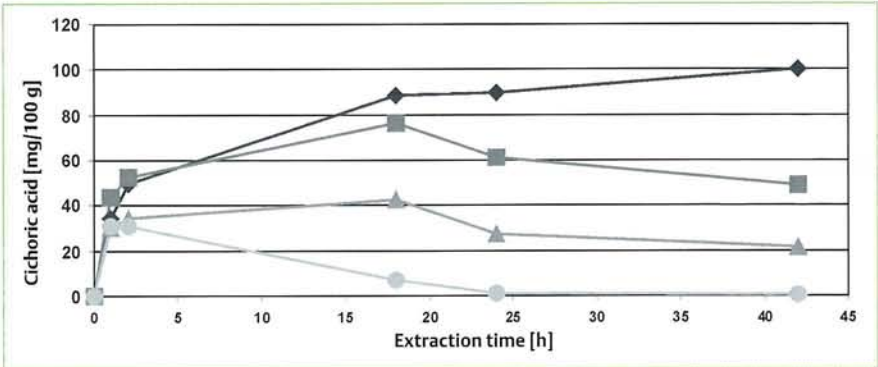
Such a market survey (**Figures 14 a/b/c**, with the related values listed in **Table 1**) shows just how different St. John's Wort preparations can be with regard to the amounts of constituents administered per day. It should be considered that all the products were examined with the same analytical methods, that the methods are validated only for the product Hyperiforce, and that differences in the product matrix could falsify the results. Products with efficacy demonstrated by controlled clinical studies are marked with an asterisk. It can be seen clearly that the daily doses of pharmacologically active constituents can differ very greatly between the products despite proven, comparable efficacy of the various products.

5. What variability is tolerable from the therapeutic point of view?

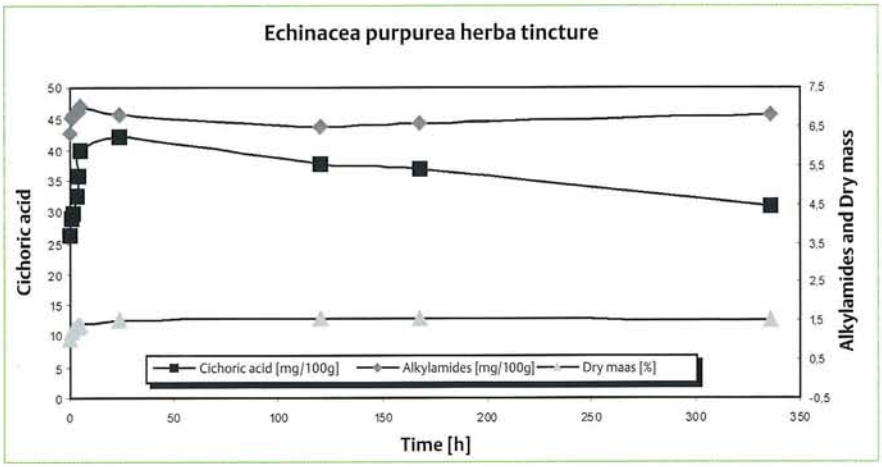
The aim of standardisation, namely to obtain similar amounts of all constituents per administered dose, can thus be achieved with natural methods.

Box 2: Variability of constituent group concentrations over several years and its reduction by the measures discussed.

	Variability of constituent group concentrations over several years (factor = highest value: low-est value)
a) Wild-collected plants	Factor 6
b) Defined plant varieties, controlled crop growth, various crop sites	Factor 3
c) As (b) and additional preparation of yearly blends of tinctures or extracts	Factor 1.5



▲ ***Figure 9: Cichoric acid extraction [mg/100 g tincture] from fresh roots of Echinacea purpurea in 60% (m/m) ethanol in relation to shredding time and atmosphere.***
◆ ***Roots shredded for 60 seconds under gassing with argon and then macerated with 60% (m/m) ethanol under gassing with argon.***
■ ***Roots shredded for 30 seconds in air and then macerated with 60% ethanol /m/m).***
▲ ***Roots shredded for 90 seconds in air and then macerated with 60% ethanol /m/m).***
● ***Roots shredded for 60 seconds under gassing with air and then macerated with 60% ethanol /m/m) under gassing with air.***



▲ ***Figure 10: Extraction kinetics for alkylamides, cichoric acid and extracted mass from Echinacea purpurea fresh herbage (60% ethanol) (data from production batches).***

A possible variation of the contents of constituent *groups* by ± 50% (corresponding to factor 3) over the years is enough when it is considered that the customer is also a natural factor and therefore shows very variable individual absorption of substances (Ziegler 1995) (Figure 13).

Differences in the pharmacokinetic parameters of medicines and variations in action curves arise through the natural law of normal distribution of biochemical features in humans also (Ziegler 1995).

Standardising herbal medicinal products should only be within the context of this variability dictated by the biochemical properties of the target groups of constituents, especially since herbal medicines are not highly active substances that have to be dosed very pre-cisely.

It is also a characteristic of herbal medicines that they exhibit a broad therapeutic safety margin, as is shown by the flatter dose-effect curves obtained in pharmacological studies of plant extracts compared to the steep curves of defined chemical substances (Hänsel 1980). The question generally arises as to whether tedious standardisation is necessary at all in the case of preparations with broader therapeutic safety margins.

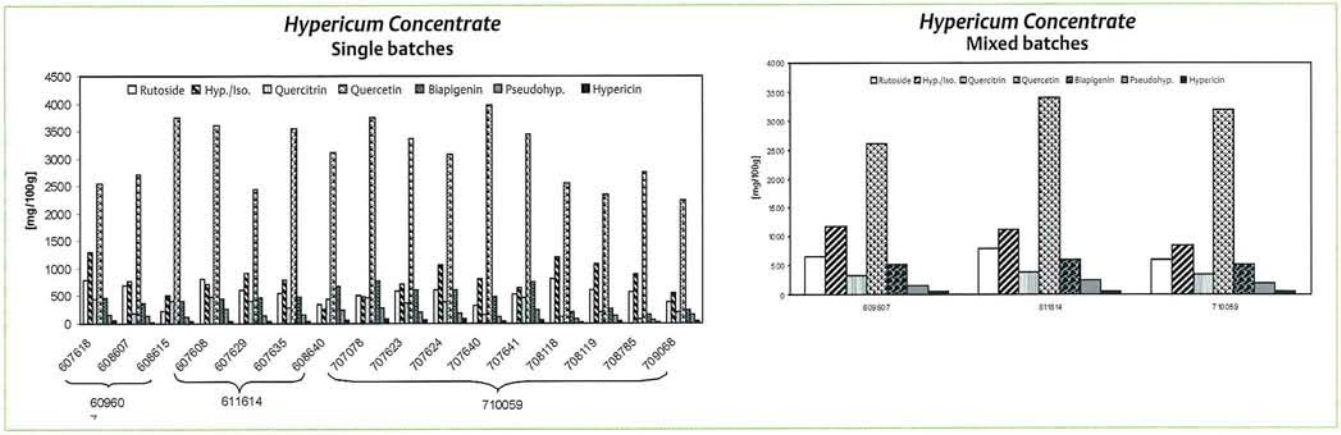
The previously readily accepted variability of herbal medicines takes full account of this circumstance. In pharmacopoeia monographs the constituent content requirements in weakly active medicinal plants are set by stating only the minimum content without stat-ing any range of variation. The German standard registration for medical infusion mixtures accepts a content variation of 20% for the individual constituents (Braun 1993). For registration application for herbal medicines in the EU, the content has to be stated with the

Box 3: Analytical values for *Hypericum perforatum* tincture from wild-collected plants (1986–1991) and the mixed batches prepared from them. The reduction of content parameter variability by this measure is clearly seen.

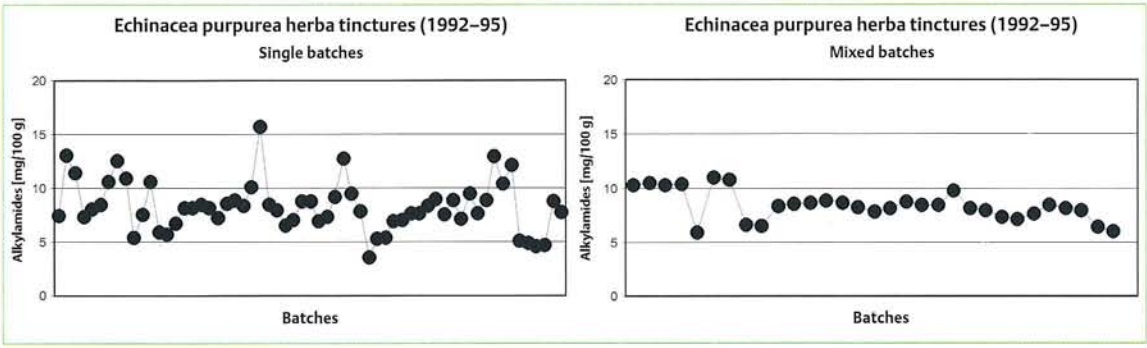
100 Individual batches		5 Yearly blends	
Flavonoid glycosides	43–240 mg/100 ml	Flavonoid glycosides	100–140 mg/100 ml
Flavonoid aglycones	24–132 mg/100 ml	Flavonoid aglycones	80–130 mg/100 ml
Hypericin derivatives	1.6–8.9 mg/100 ml	Hypericin derivatives	4.9–8.2 mg/100 ml
Extract content	1.9–3.7%	Extract content	2.4–3.3%

Table 1: Comparison of St. John's Wort products on the European market.

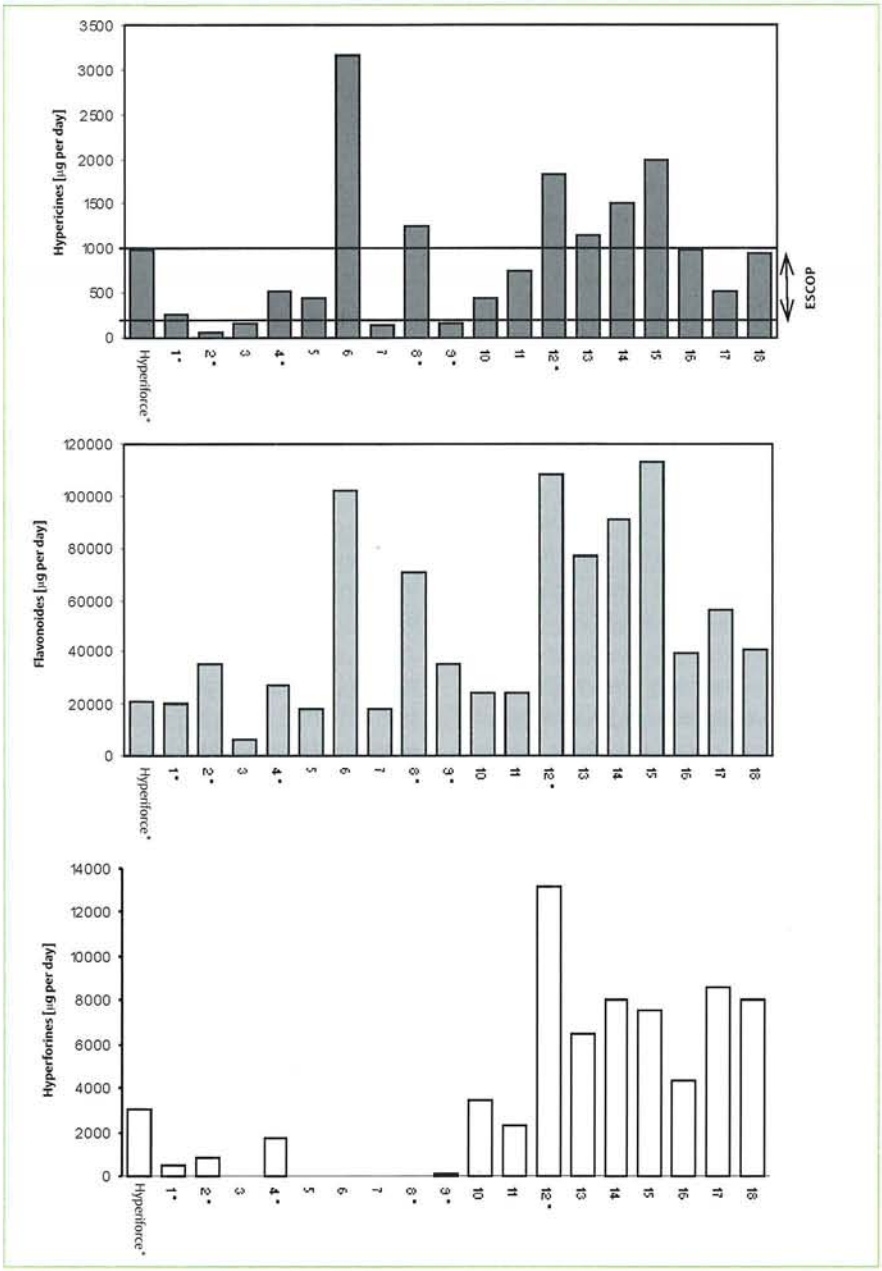
Product	Origin	Dose (per day)	Hypericines (µg/day)	Flavonoides (µg/day)	Hyperforines* (µg/day)	Status	Clin. Study Y/N
Hyperi-force	CH	3 x 1	990	21'000	3'000	reg.	Y
1	DE	2 x 1	266	20'400	500	reg.	Y
2	DE	3 x 1	63	35'700	810	reg.	Y
3	CH	3 x 1	165	6'000	< 10	reg.	N
4	DE	2 x 1	530	27'200	1'720	reg.	Y
5	NL	3 x 1–2	439	18'000	< 10	?	N
6	DE	3–4 x 1–3	3'156	102'000	< 10	reg.	N
7	DE	2 x 1	136	18'200	26	reg.	N
8	CH	2 x 1	1'240	71'000	< 10	reg.	Y
9	DE	1–2 x 1–2	160	35'600	52	reg.	Y
10	SE	2 x 1	448	24'600	3'460	?	N
11	FI	1–2 x 1	752	24'200	2'320	?	N
12	DE	2–3 x 1	1'830	108'000	13'200	?	Y
13	AU	3 x 1	1'140	76'800	6'480	?	N
14	AU	3 x 1	1'500	91'200	8'010	?	N
15	US	2 x 1	2'000	113'000	7'500	?	N
16	NO	1 x 1	983	39'400	4'300	?	N
17	PT	2 x 1–2	532	56'400	8'560	?	N18
18	PT	2 x 1	952	40'800	8'060	?	N



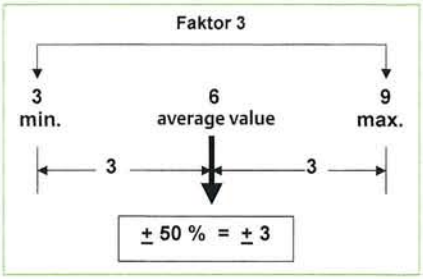
▲ ***Figures 11 a+b: Constituent concentrations of 16 production batches of Hypericum extract (data over 2 years) pooled to give blended batches.***



◀ *Figures 12 a+b: Comparison between constituent concentrations of individual batches of Echinacea herbage tinctures and of blended batches.*



▲ *Figures 14 a+b+c: Comparison of St. John's Wort products on the European market with regard to the daily doses of constitutents. Products whose efficacy has been demonstrated by controlled clinical studies are marked with an asterisk.*



▲ *Figure 13: Schematic description to convert factor of fluctuation to percentage*

least possible tolerance (75/318/EEC, 1997), i.e. the data can be determined on a product-specific basis. In the latest Note for Guidance on Specifications, no statement is now made on the topic of variability (EMEA 1999). As an example of a plant preparation with considerable side effects potential, the "Adjusted senna leaf dried extract" Ph. Eur. may be considered. Apart from an analytical variability of ± 10 %, a variation of sennoside content by a factor of 1.45 between the highest and lowest values is accepted. The data presented in this article also lie within this range.

It is often stated that with the use of cloned plants all containing exactly the same genetic code standardisation could be enhanced. However, even then the effects of ecological factors at different growing sites on quality would still remain. The growing of cloned plant crops is very risky. If one plant is diseased, the risk of contagion is much higher in the case of genetically identical plants. The spread of cloned crops would also lead to dilution of the genetic variability available in agriculture, coupled with increased environmental

contamination through increased plant treatment procedures.

So-called special extracts with fewer plant constituents than total extracts (e.g. 500 instead of 10,000) could be standardised more easily since they are less complex. However, with these partially enriched extracts we become far removed from the plant. They are more like contaminated pure substances.

This special extracts have probably been developed because they are much less complex and so can be better dealt with scientifically. They can be linearly characterised by quantitative analytical methods. However, this can be achieved only at the price of a radical elimination of complexity. But since nature is very complex, we should sensibly deal with complexity. This means recognising *all* the facts and being satisfied with probabili-ties, orders of magnitude and qualitative statements. A concentration variation factor of at least 3 should be therefore have to be assumed for the individual constituents. *It should also be sufficient to standardise on constituent groups and not on individual, chemically defined constituents.* To quantify all known substances of a medicinal plant an inordinately great analytical effort would be necessary.

Market monitoring also clearly shows a new trend toward "fashionable constituents" and "enrichment" of extracts going far beyond the requirements of the official German Commission-E Monographs based on traditional use (Blumenthal 1998). This could be the reason for the recent appearance of previously unknown side effects.

In summary, it therefore remains to be established that, due to the lack of understanding of the efficacy of their complex composition, herbal medicines cannot be compared directly with chemically pure substances. It is thus sensible to remember the basics, and so we continue to strive to prepare herbal medicines with total extracts from natural plants and to standardise them as far as is necessary and as far as nature allows.

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Summary

Standardisation of herbal medicine – the natural way

All living creatures are influenced by the law of natural variability. By standardising herbal medicinal products, the uniformity of contents is also affected by this law due to the natural starting material. With an example of herbal medicine from fresh plants, factors influencing the contents of active ingredients are demonstrated. The variability of quality parameters depends on genetic properties of the plants, the ecological conditions during vegetation period and the manufacturing process. Even under optimal conditions, the fluctuation latitude of the contents is hardly below 50 percent, a factor that has hitherto been accepted as tolerable. Nonetheless, registration authorities examine drug applications of herbal medicinal products in the same manner as chemical drugs in spite of this deviation. It is shown by means of examples in this article that this is not possible and necessary out of natural reasons as well as from the viewpoint of therapy, especially when dealing with complex mixtures of medicinal plant products.

Key words

Herbal medicinal products, standardisation , natural variability, uniformity of contents, fresh plant products, medicinal plant cultivation.