

# New WHO Guideline and EC Directives on Traceability of Herbal Raw Material: A Chance for the Amelioration of Quality and Safety of Medicinal Plant Raw Material



Schmidt, M.\*, Thomsen, M.\*\* and Betti, G.\*\*\*

\* Herbresearch, Im Westfeld 29, D-33428 Harsewinkel, Germany

\*\* Graduate School of Integrative Medicine, Swinburne University of Technology, Melbourne, Australia,

\*\*\* Medicinal and Aromatic Plants R&D, 2000 Rte des Lucioles, F-06901 Sophia Antipolis, France



## Introduction

Currently, most herbal raw materials are still harvested or wild crafted under completely uncontrollable conditions (Lange 2004). The risk of adulteration is only one aspect of the problem – all discussions regarding efficacy and toxicological aspects of medicinal plants are of questionable value if a consistent and reproducible quality of the raw material cannot be achieved. Additionally, in cases of adverse events caused by poor plant quality, producers who insist on quality control will suffer as much as those who have created the problem by using inadequate controls in the first place.

New guidelines affecting the collection of herbal plant raw material are currently being implemented within the EU countries. EC directives 178/2002/EC and NTA Vol 2B Ed. July 2003 regulate the traceability of herbal raw materials for food and drug use, and the WHO guideline "Good Agricultural and Collection Practice" is defining the rules by which the herbal material should be collected (WHO 2003). Both guidelines, traceability and collection practice, should lead to total transparency of the whole chain of production of most herbal medicines from the plant, down to the finished product.

Major consequences of the new guidelines will be:

- Unambiguous botanical identification of medicinal plants
- Selection of cultivars tailored to the use of the final product
- Decreasing danger of adulterations, and thus of accidental toxicity
- Amelioration of the reproducibility of the clinical effects of herbal medicines
- Protection of the environment.

In anticipation of the new regulations we are establishing full traceability for a range of medicinal plants, paired with selection of high performance cultivars and, wherever possible, bioorganic cultivation.

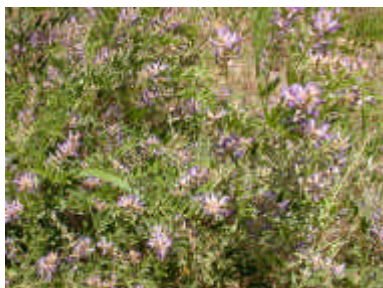
## Unambiguous botanical identification

There is no guarantee that a plant species labelled on the package of a product is really used in its production.

### Example: *Glycyrrhiza glabra*

Depending on the origin and – most important – the trading paths, liquorice labelled "*Glycyrrhiza glabra* Ph. Eur." can contain more or less high amounts of other *Glycyrrhiza* species, especially the Russian form *G. uralensis* (Schöpke 2003).

In our cultivation project in Iran, traceability and reproducibility of high quality *Glycyrrhiza glabra* was easy to achieve.



*Glycyrrhiza glabra* (Iran)

### Example: *Equisetum arvense*

Many different species are collected under the name "arvense" (Hiemann 2003), among them potentially toxic species such as *Equisetum palustre* (Veit 1987). Achieving traceability for *Equisetum arvense* was part of a large project organized by our working group. The material supplied by Herbresearch now comes from a GACP conforming cultivation in France on fields specially dedicated to horsetail. A bio-organic production without the use of herbicides and pesticides is possible.

### Example: *Eleutherococcus senticosus*

Striking examples for the need of quality standards in botanical identification can be found in the literature on phytovigilance. An example is the adulteration of *Eleutherococcus senticosus* with *Periploca sepium*, caused by a misinterpretation of the Chinese traditional plant name "wu-jia-pi" and an obvious lack of quality control (Awang 1996). The great danger with such events is that – though unrelated to the labelled species – the adverse effect often finds its way into package leaflets and the warnings therein. Our project to ensure traceability of herbal raw material also includes *Eleutherococcus senticosus*. Currently a number of different origins are evaluated.



*Eleutherococcus* sp. (experimental cultivation)

### Example: *Harpagophytum procumbens*

Erroneous botanical identification is often deliberately maintained for economic or political reasons. One obvious example is Devil's claw, which according to the European pharmacopoeia is the Namibian

species *Harpagophytum procumbens*. The roots of this plant are deliberately mixed with roots of a related species, *Harpagophytum zeyheri*, growing in Angola. A major reason for this exchange is the growing demands of wild-crafted roots, surpassing the capacity of natural regeneration of *Harpagophytum procumbens* in Namibia, and the much lower price for raw material from Angola. Currently, more than 50% of imported roots labelled as "*Harpagophytum procumbens*" are in effect *Harpagophytum zeyheri*, with increasing tendency (Schmidt et al. 1998). Even though this does not pose problems from the toxicological point of view, the situation puts the validity and reproducibility of former clinical trials into jeopardy, as one cannot simply assume a pharmacological or clinical equivalence of both species. Full traceability of *Harpagophytum procumbens* with a high content in harpagoside can already be guaranteed in our project.

## Selection of cultivars

The fact that a plant is cultivated does not automatically imply that it is of suitable quality for pharmaceutical use. The phytochemical characteristics should be defined according to the envisaged use of the plant.

### Example: *Thymus vulgaris*

There are at least seven major thyme chemotypes (*Thymus vulgaris*) with either carvacrol, geraniol, linalool, a-terpineol, trans-thujanol, 1,8-cineol or thymol as the major component of the essential oil (Stahl-Biskup 2003). These chemotypes show a distinct variability according to their origin. Thus, the cineol type can be found in Spain, but not in France, whereas the geraniol type could not be obtained from Spain (Stahl-Biskup 2003). The use of the chemotype must affect the efficacy of the preparation. In pharmacological experimentation the antimicrobial activity of thymol-types was greatest, followed by carvacrol. A defined origin and composition of the chemotype would greatly add to the reproducibility of the effects of thyme preparations. In our project, we ensure that we are using a consistent supply of one defined thymol chemotype.



*Thymus vulgaris* (France)

### Example: *Calendula officinalis*

Cultivar selection according to pharmacological and toxicological aspects is only possible when the active ingredients or potentially toxic compounds are known. Where this is not the case, traceability projects must take the botanical variability into account. We approached the issue of *Calendula officinalis* by planning dedicated cultivations on diverse sites in different countries, but with all sites using a plant type with an essentially similar overall quality.



*Calendula officinalis* (Iran)

### Example: *Chamomilla recutita*

The selection of suitable sites must also take the geological conditions into account. Thus, we found better results for the cultivation of selected chamazulene-types of chamomile (*Chamomilla recutita*) on karstic substrate. In the end, the choice of a cultivar is always a compromise between biomass, resistance against plant diseases, and phytochemical composition. We attempt to approach all these factors systematically.



*Chamomilla recutita* (Iran)

## Protection of the environment

The current practice of wild crafting is, more often than not, creating havoc to the environment. For example, in Turkmenistan some international companies lower their costs and increase the turnovers by harvesting liquorice root (*Glycyrrhiza glabra*) using heavy agricultural machinery, concomitantly spoiling the prices for those who collect conventionally and continue to create sustainable employment in the countries of origin. As a consequence, in the regions where this kind of collection method is practised, not only is environment badly damaged, but also the plant is deprived of all possibilities for natural regeneration. It is foreseeable that the supply will be finite. As a plant becomes endangered, the danger of adulterations increases parallel to the decreasing plant density in its natural habitats. Controlled cultivation of collection projects under the rules of GACP will not only ensure the sustainability of raw material supply, but also improve quality and reproducibility – and of course, drug safety.



Hundreds of tons of roots of *Glycyrrhiza glabra* are processed every year

## Herbs with traceable quality

Our project of ensuring traceability and selection of high quality plant material was so far successful for the following plants:

Aesculus hippocastanum	Melissa officinalis
Allium sativum	Opuntia ficus-indica
Arctium lappa	Passiflora incarnata
Calendula officinalis	Sambucus nigra
Chamomilla recutita	Solidago virgaurea
Cimicifuga racemosa	Taraxacum officinale
Crataegus sp.	Thymus vulgaris
Cynara scolymus	Valeriana officinalis
Echinacea purpurea	Viola tricolor
Equisetum arvense	Vitex agnus-castus
Hamamelis virginiana	
Harpagophytum procumbens	<b>In progress:</b>
Helichrysum italicum	Rhodiola rosea
Humulus lupulus	Eleutherococcus senticosus

## Conclusions

The new rules for traceability of herbal raw material and good agricultural and collection practice will lead to an improvement in the predictability of herbal drug quality. Simultaneously, an increased reproducibility of pharmacological effects and clinical efficacy can be expected, and the danger of accidental intoxications through adulterants will diminish.

As many companies are as yet unaware of the practical consequences of the new regulations, the implementation into national law might create confusion and will surely imply practical problems. With a proper planning, such problems can be overcome. We are currently successfully ensuring traceability for 25 different medicinal plants. Approximately 20 more medicinal plants will be added within the next 12 months.

## References

- Awang, D. V. C. (1996). Siberian ginseng toxicity may be case of mistaken identity. *Can.Med.Assoc.J.* 155: (9) 1237
- Hiemann, A. (2003). *Equisetum*. In: Blaschek, W., Ebel, S., Hackenthal, E., Holzgrabe, U., Keller, K., and Reichling, J.: *HagerROM 2003 V. 4.1.* Hagers Handbuch der Drogen und Arzneistoffe. Heidelberg: Springer Electronic Media.
- Lange, D. (2004). Medicinal and Aromatic Plants: Trade, Production, and Management of Botanical Resources. In: Cracker, L. E., Simon, J. E., Jatsiatien, A., and Lewinsohn, E.: *XXVI International Horticultural Congress: The Future for Medicinal and Aromatic Plants.* Toronto, Canada: ISHS Acta Horticulturae, 177-197.
- Schmidt, M., Eich, J., Kreimeyer, J., and Betti, G. (1998). Anbau der Teufelskralle. Ein Projekt in Namibia zur Sicherung der pharmazeutischen Qualität. *Dtsch.Apoth.Ztg.* 138: (47) 4540-4549.
- Schöpke, T. (2003). *Glycyrrhiza*. In: Blaschek, W., Ebel, S., Hackenthal, E., Holzgrabe, U., Keller, K., and Reichling, J.: *HagerROM 2003 V. 4.1.* Hagers Handbuch der Drogen und Arzneistoffe. Heidelberg: Springer Electronic Media.
- Stahl-Biskup, E. (2003). *Thymus*. In: Blaschek, W., Ebel, S., Hackenthal, E., Holzgrabe, U., Keller, K., and Reichling, J.: *HagerROM 2003 V. 4.1.* Hagers Handbuch der Drogen und Arzneistoffe. Heidelberg: Springer Electronic Media.
- Veit, M. (1987). *Di.Apoth.Ztg.* 127: 2049-2056.
- World Health Organization (2003). WHO guidelines on good agricultural and collection practices (GACP). Geneva.