



Data elements and structures for the unique identification herbal medicinal products

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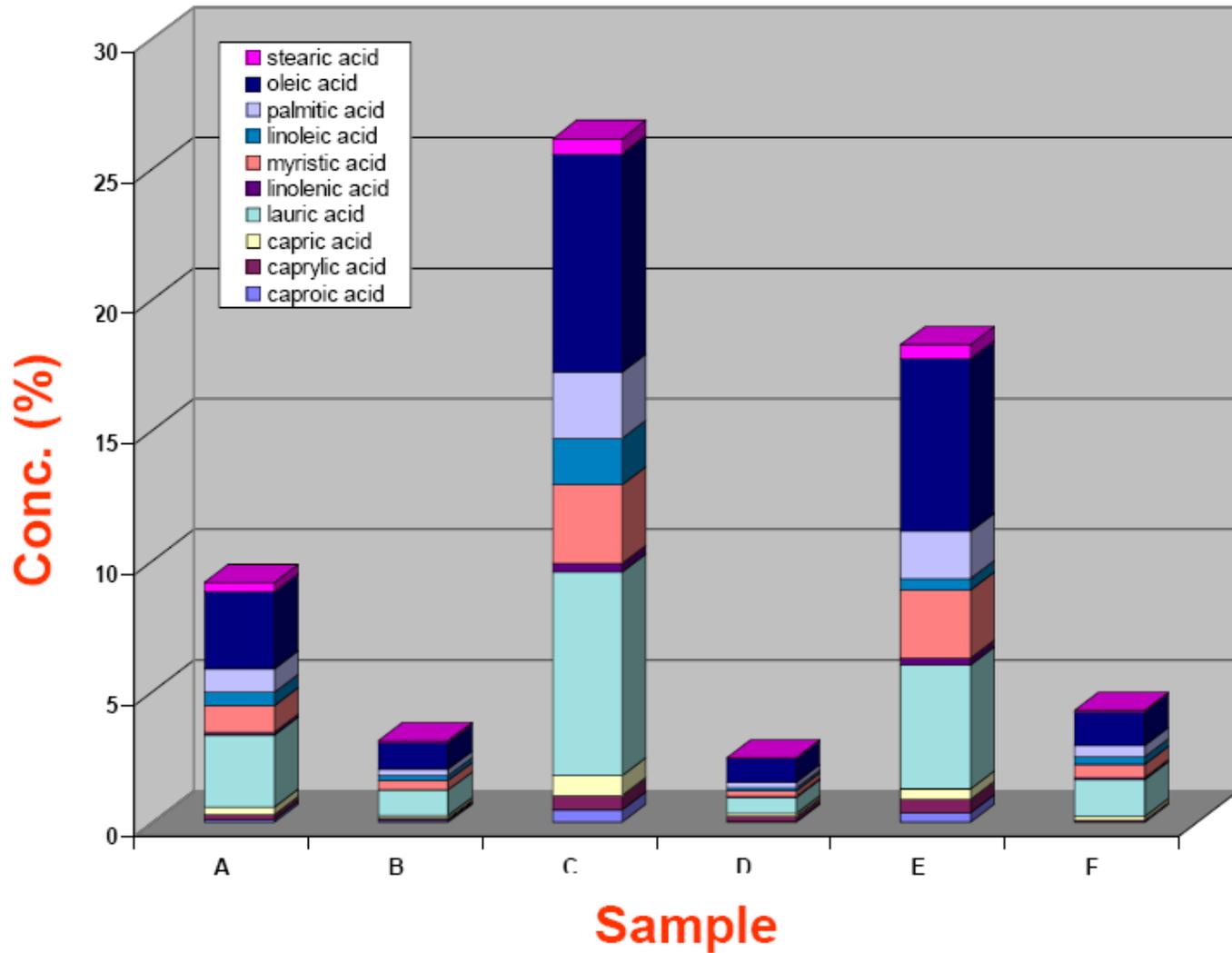
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$$\begin{array}{r} C \quad B \quad G \\ \hline M \quad E \quad B \end{array}$$

MEDICINES
EVALUATION
BOARD

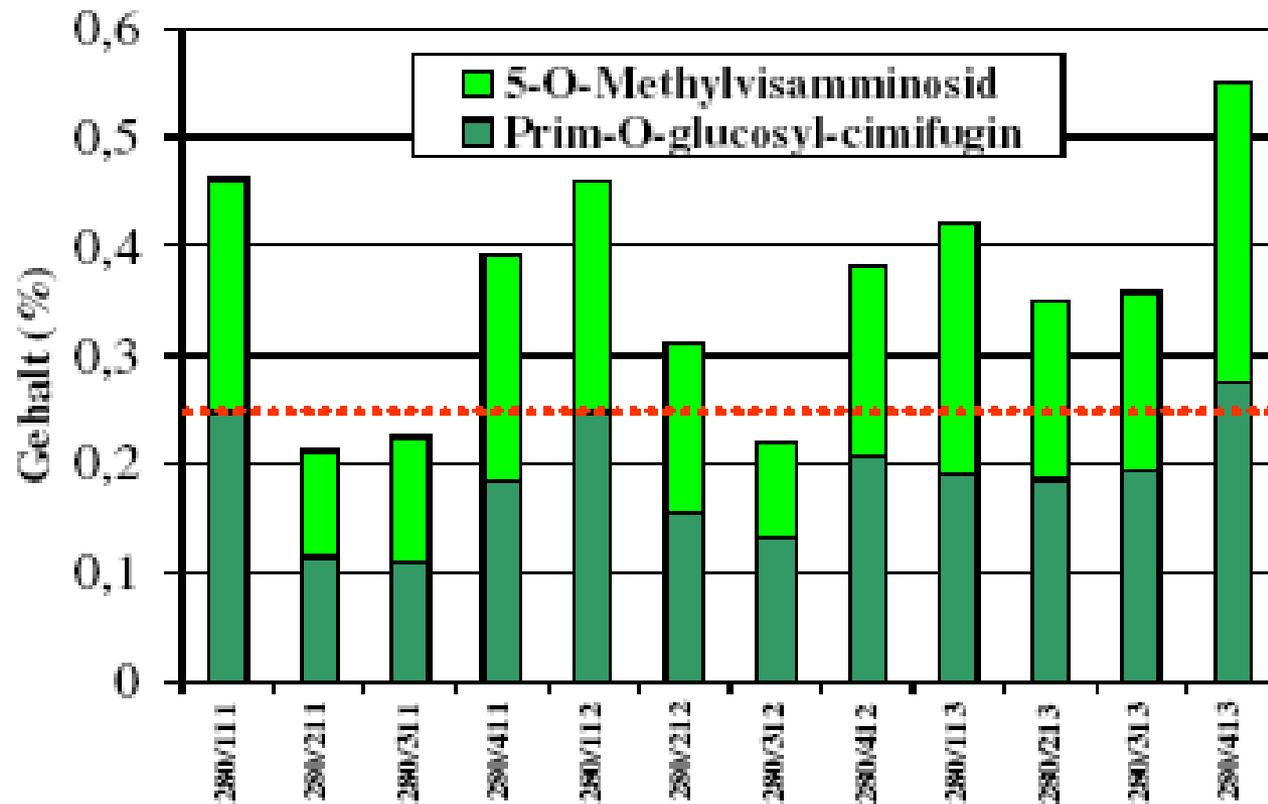
Definition of herbal medicinal products 2004/24/EC

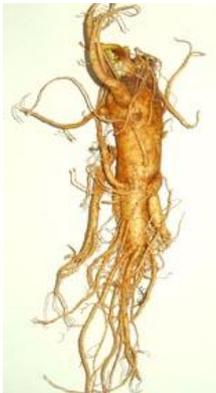
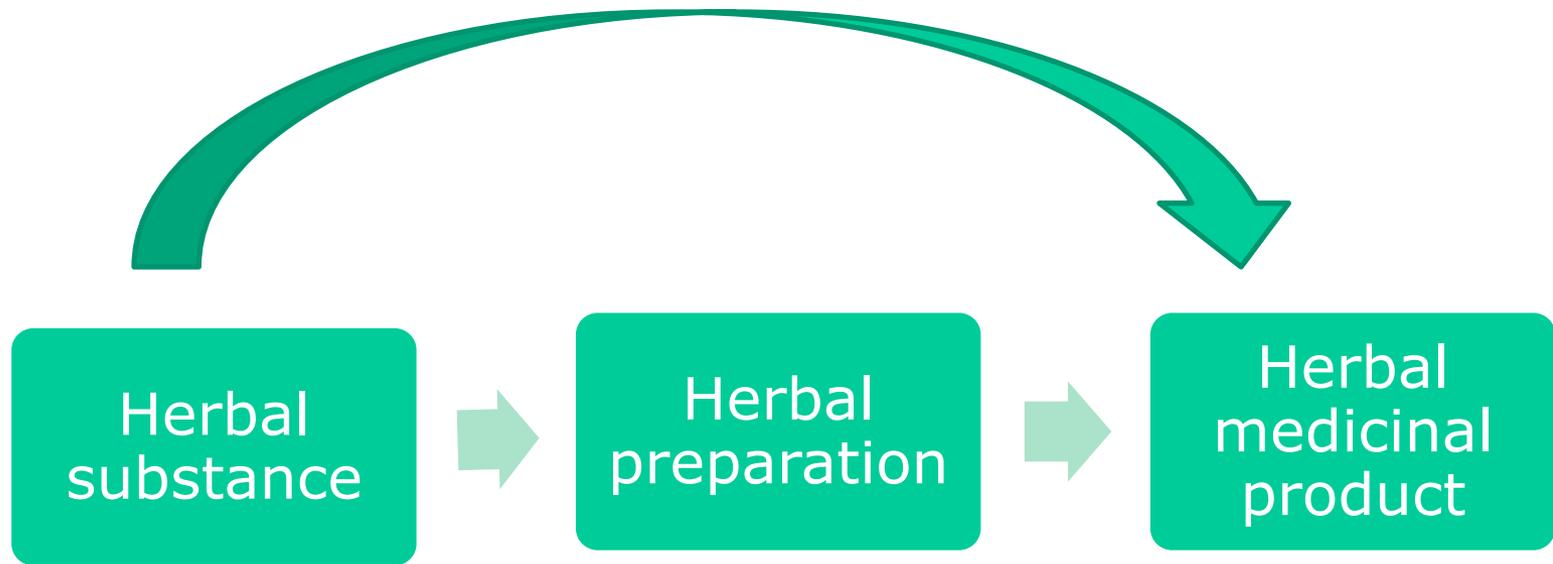
Herbal medicinal products: any medicinal product, *exclusively* containing *as active substances* one or more *herbal substances* or one or more *herbal preparations*, or one or more such herbal substances in combination with one or more such herbal preparations



Saposhnikoviae radix - Fangfeng

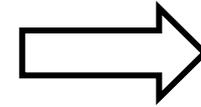
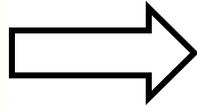
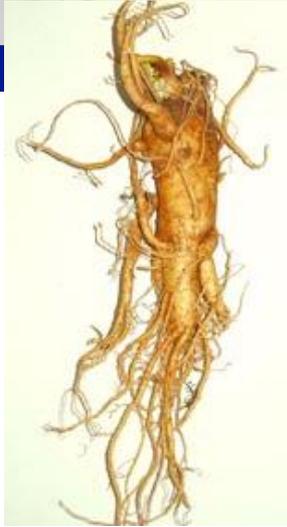
Ernte 2005





2003/63/EC Preamble (8)

“Herbal medicinal products differ substantially from conventional medicinal products in so far as they are **intrinsically associated with** the very particular notion of **herbal substances and herbal preparations**. It is therefore appropriate to determine **specific requirements** in respect of these products with regard to the standardised marketing authorisation requirements.”



Herbal substance

- cultivation/harvesting /drying conditions
- Microbial levels, aflatoxins, heavy metals etc)
- Pre-post-harvest chemical treatments (pesticides fumigants)

Herbal Preparation

- Methods of preparations
- Drying conditions (microbial levels)
- Microbial purity on storage

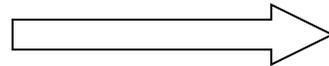
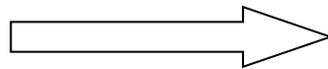
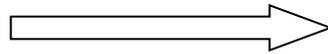
Herbal Medicinal Product

- Manufacturing process (temperature effects, residual solvents)
- Profile and stability of the active constituents
- formulation in packaging

Quality assurance of herbal medicinal products

Quality assurance

- Ensure that that the right plant (part) is used
- Absence of impurities
- Appropriate levels of active constituents and batch to batch consistency



Quality control

- Clear botanical definition
- Test for identity
- Test for purity
 - Adulteration
 - Foreign materials
 - Fumigants
 - Mycotoxins
 - Pesticides
 - Toxic metals
 - Microbial contamination
 - Residual solvents
- Assay for constituents with known therapeutic activity or (active) markers

European Pharmacopoeia classification of Herbal extracts

- “*Standardized extracts*”: Constituents responsible for the therapeutic activity are known.
- “*Quantified extracts*” No constituents with known therapeutic activity but active markers.
- “*Other extracts*” Active constituents not known.



QUALITATIVE AND QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCE(S) OF A HERBAL MEDICINAL PRODUCT

- **Standardised herbal substances / herbal preparations** are adjusted to a given content of constituents with known therapeutic activity within an acceptable tolerance; standardisation is achieved by adjustment of the herbal substances/herbal preparations with **excipients or by blending batches** of herbal substances and/or herbal preparations.

Example:

Sennae folium 415-500 mg, corresponding to 12.5 mg of hydroxyanthracene glycosides, calculated as Sennoside B





QUALITATIVE AND QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCE(S) OF A HERBAL MEDICINAL PRODUCT

- **Quantified herbal substances/herbal preparations** are adjusted to a defined range of constituents (active markers); **adjustment is exclusively achieved by blending batches** of herbal substances and/or herbal preparations.

Example:

Salicis cortex 4 g, corresponding to 40 to 48 mg of total phenolic glycosides, expressed as salicin





QUALITATIVE AND QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCE(S) OF A HERBAL MEDICINAL PRODUCT

- **Other** herbal substances/herbal preparations are active substances for which neither constituents with known therapeutic activity nor active markers are known. These herbal substances/herbal preparations are **not adjusted** to a defined content of analytical marker.

Example:

Valerianae radix 900 mg



Important data elements for the unique identification the **herbal substance**

- Botanical name (incl. author and varieties)
- Hybrids /varieties/cultivars?

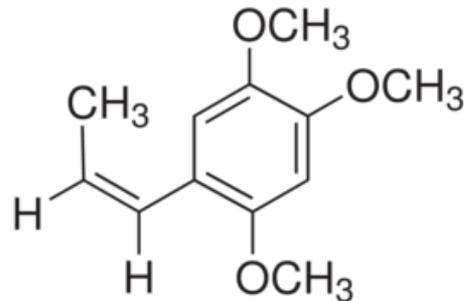
β asarone content of *Acorus calamus* varieties

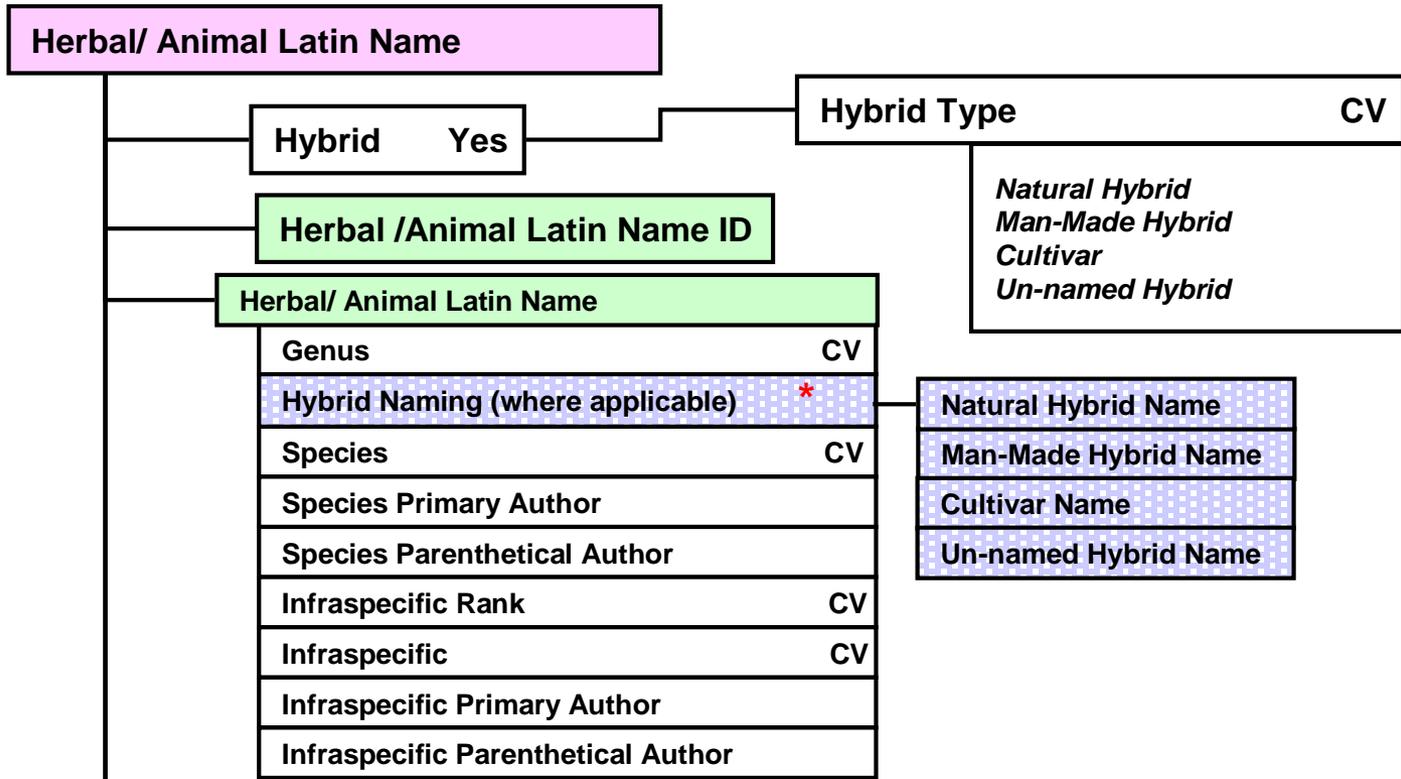


var. *americanus* (Raf) Wulff (Diploid) Rt:ND, Eo: ND

var. *calamus* (triploid) Rt: 0,3%, Eo:19%

var. *Angustatus* (Bess) (tetraploid) Rt: 8.3%, Eo: 95%





Important data elements for the unique identification the **herbal substance**

- Botanical name (incl. author and varieties)
- Origin
- Common name

Herbal/ Animal Latin Name

Hybrid Yes

Hybrid Type CV

- Natural Hybrid*
- Man-Made Hybrid*
- Cultivar*
- Un-named Hybrid*

Herbal /Animal Latin Name ID

Herbal/ Animal Latin Name	
Genus	CV
Hybrid Naming (where applicable) *	
Species	CV
Species Primary Author	
Species Parenthetical Author	
Infraspecific Rank	CV
Infraspecific	CV
Infraspecific Primary Author	
Infraspecific Parenthetical Author	

- Natural Hybrid Name
- Man-Made Hybrid Name
- Cultivar Name
- Un-named Hybrid Name

Local Herbal/Animal Name Description	
Local Binominal Name	
Reference Country	CV
Accepted Name	Y/N
Cited Name	Y/N

According with Herbal/ Animal Latin Name

Hierarchy Level CV
Link to Parent CV

Reference Source CV

Common Herbal/Animal Name Description	
Common Name	CV
Language Code	CV

* Hybrid Naming applies when the herbal/animal is a hybrid

Fangji



Han Fangji

- More than 100 cases of nephropathia („Aristolochia nephropathia“)
- More 40 women are being dialysed.
- Cancer



Guang Fangji

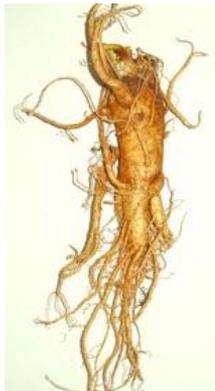
Important data elements for the unique identification the **herbal substance**

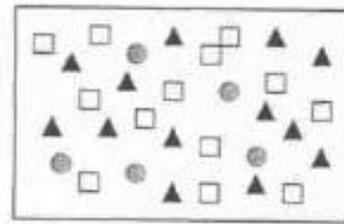
- Botanical name (incl. author and varieties)
- Common name?
- Origin?
- Plant part used
- Growth stage
- Processing Fresh/dried
- Reference (*e.g* Pharmacopoeia)
- markers

Herbal
substance

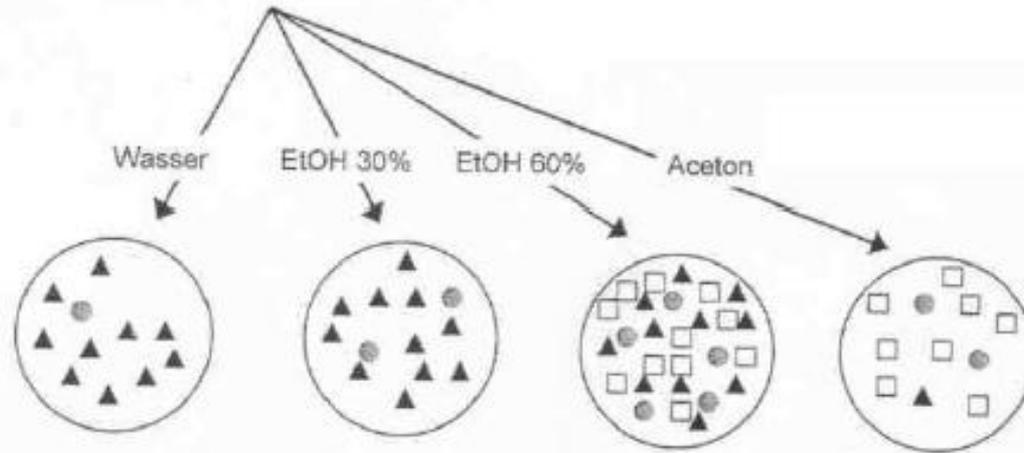


Herbal
preparation





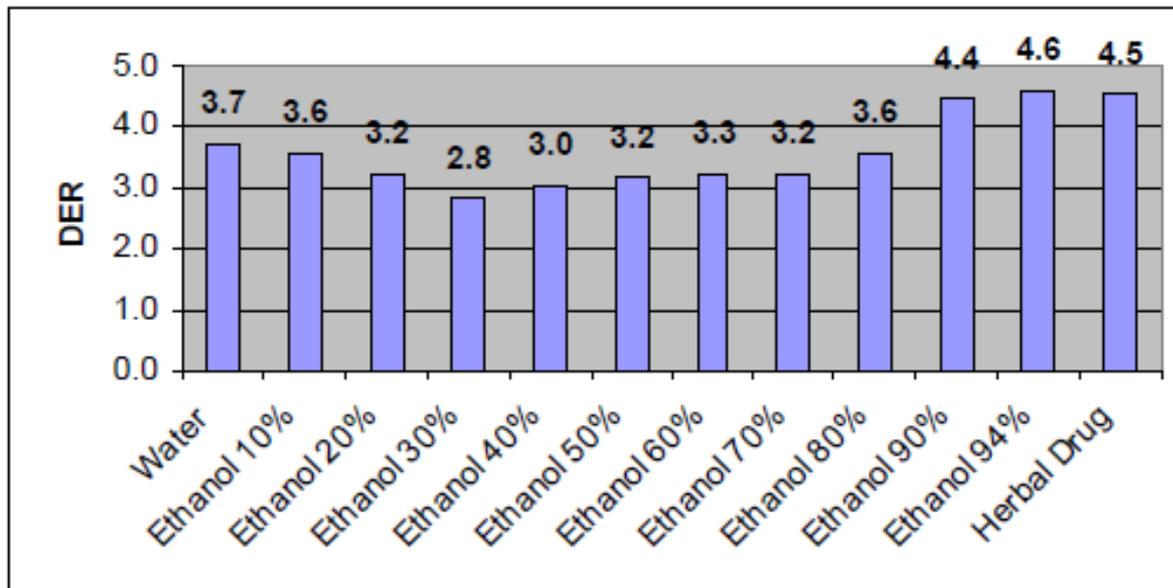
Starting material:
Herbal drug:
A multi component system



Different extracts

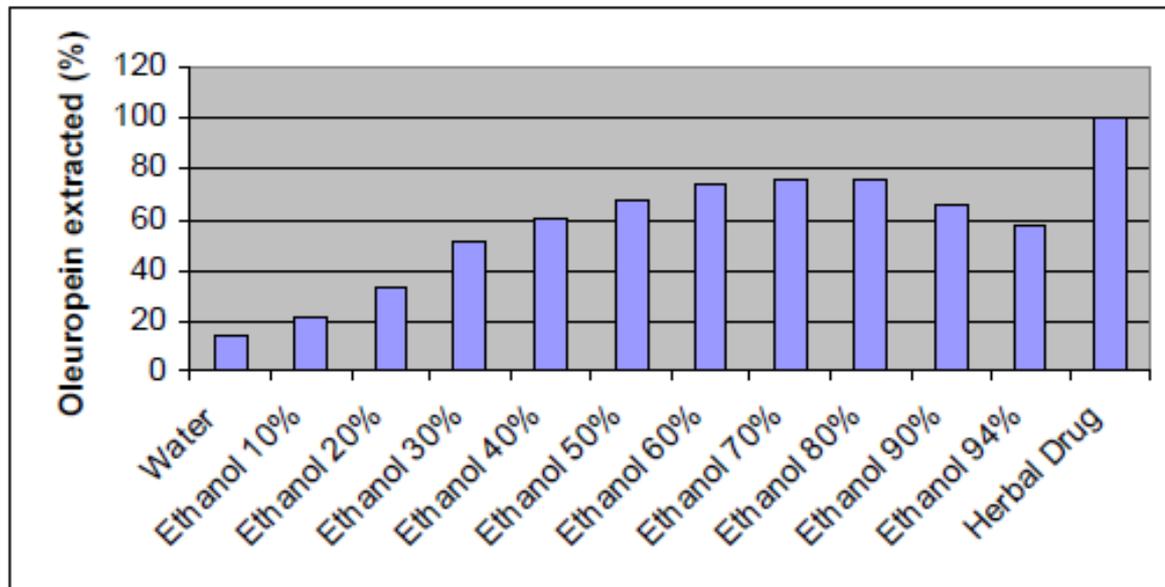
Solvent: 65-96 per cent V/V ethanol

Drug extract ratio



Solvent: 65-96 per cent V/V ethanol

Extraction profile for oleuropein



Import data elements for the unique identification the
herbal preparation (*e.g.* extract)

- Preparation method
- Extraction solvent
- Drug to Extract Ratio (DER)
- Markers/ reference compounds
- Reference (*e.g.* Pharmacopoeia)
- Excipients

MARSHMALLOW ROOT

Althaeae radix

DEFINITION

Peeled or unpeeled, whole or cut, dried root of *Althaea officinalis* L.

IDENTIFICATION

A. The unpeeled, non-fragmented drug consists of cylindrical, slightly twisted roots, up to 2 cm thick, with deep longitudinal furrows. The outer surface is greyish-brown and bears numerous rootlet scars. The fracture is fibrous externally, rugged and granular internally. The section shows a more or less thick, whitish bark with brownish periderm, separated by the well-marked, brownish cambium from a white xylem. The stratified structure of the bark and the radiate structure of xylem become more distinct when moistened.

The peeled drug has a greyish-white, finely fibrous outer surface. Cork and external cortical parenchyma are absent.

▶ B. Microscopic examination (2.8.23). The powder is greyish-brown (unpeeled root) or whitish (peeled root). Examine under a microscope using [chloral hydrate solution R](#). The powder shows the following diagnostic characters (Figure 1126.-1): fragments of colourless, mainly unligified, thick-walled fibres [C, D, M] with split or pointed ends [D], sometimes accompanied by parenchymatous cells of the medullary rays [M], or grouped [C]; fragments of vessels, bordered-pitted or with reticulate or scalariform thickenings [G, H]; cluster crystals of calcium oxalate about 20-35 µm, mostly 25-30 µm in size, isolated [K] or included in parenchymatous cells [B]; fragments of parenchyma [E] with cells containing mucilage [Ea, F]; fragments of cork with thin-walled, tabular cells in surface view [A] and transverse section [L] (unpeeled root). Examine under a microscope using [ruthenium red solution R](#). The powder shows groups of parenchyma containing mucilage, which stains orange-red.

3.2.S.2.6.1 Herbal Substance

Marshmallow root, peeled consists of the whole or cut, dried roots of *Althaea officinalis* L. The harvesting time is from autumn to spring during the dormant season by wild collections or cultivations in Europe. The material is dried and cut coarse prior to extraction. The herbal substance, marshmallow root has to comply with the currently valid EP monograph. The resulting aqueous extract of marshmallow root (1 : 19.5 - 23.5) is a clear to light cloudy yellowish liquid with a faint fruity odor.

3.2.S.2.6.2 Herbal Preparation

The manufacturing of the herbal preparation extract of marshmallow root (1 : 19.5 - 23.5) is a standard procedure described in the German Drug Codex (DAC). For the the content of the aqueous extract of marshmallow root (1 ; 19.5 - 23.5) the L-alanine content is specified. The amino acids are characteristic substances included in the extract preparation. The content of L-alanine in the aqueous extract of marshmallow root is specified with 10-50 ng/g. The aqueous macerate of marshmallow roots is not stable. It is directly boiled with saccharose to produce the syrup.

SmPC section 2

2. KWALITATIEVE EN KWANTITATIEVE SAMENSTELLING

100 g (= 76,44 ml) stroop bevat 35,61 g *Althaea officinalis* L., wortel (heemstwortel) extract (1 : 19,5-23,5).

Extractiemiddel: gezuiverd water.

Information from the Registration Dossier

3.2.S.1.1 Nomenclature

Scientific name of the plant, with the name of the authority, variety and chemotype (where applicable):	Marshmallow root (<i>Althaea radix</i>)
Parts of the plant:	Marshmallow root consists of the peeled or not peeled, whole or cut, dried roots of <i>Althaea officinalis</i> L.
Definition of the herbal drug preparation:	Extract of marshmallow root (1 : 19.5 - 23.5)
Ratio of the herbal drug to the herbal drug preparation:	(1 : 19,5 - 23.5)
Extracting agent:	purified water
Primary processing:	drying and cut coarse
Storage:	protected from light

3.2.S.2.2.1 Specification Herbal substance

English title:	Marshmallow root, peeled
German title:	Eibischwurzel, geschält
Monograph:	EP 1126
Latin subtitle:	<i>Althaeae radix</i>
Botanical name (authority):	<i>Althaea officinalis</i> L.
Origin:	Europe, in particular Poland, Hungary and Serbia
Method of production:	Wild collections and cultivation
Harvesting period:	From autumn to spring, during the dormant season
Primary processing:	Washing with water, drying, peeling and cut coarse
Storage conditions:	Cool, dry and protected from light

Information from the Registration Dossier

3.2.S.1.2 Structure

Extract of marshmallow root (1 : 19.5 - 23.5) is a clear to light cloudy yellowish liquid with a faint fruity odor. It contains 10 - 50 µg/g of L-alanine.

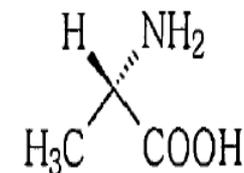
German name: L-Alanin

English name: L-alanine

IUPAC-name: (2S)-2-aminopropionic acid

Synonyms: α-aminopropionic acid

Structure:



Class: *Substance (readonly)*

Property	Value
CBG Number:	
CAS Number:	0073049657
* Dutch Name:	ALTHEA WORTEL WATERIG EXTRACT (19,5-23,5 =1)
Homeopathic Name:	
Preferred Term As Inactive Ingredient:	
Quantity Indicator Inactive Ingredient:	
P RMS:	
Harmonised Substance Data Lock Point:	
Active Ingredient Synonym:	"Marshmallow (<i>Althaea officinalis</i> , ext.); "Aqueous extract (1:19,5-23,5) of the peeled whole or cut dried root of <i>Althaea officinalis</i> L."; "Waterig extract van heemstwortel (1:19,5-23,5)"
Origin:	
Latin Name:	ALTHAEAE RADIX EXTRACTUM LIQUIDUM
INN Name:	ALTHAEAE RADIX EXTRACT
English Name:	MARSHMALLOW ROOT EXTRACT (1= 19,5-23,5)
Inactive Ingredient Name:	
Notes:	Aqueous extract (1= 19,5-23,5) of the peeled whole or cut dried root of <i>Althaea officinalis</i> L. The roots are macerated with water at room temperatur for 2 hours. After separation of the macerate and pressing of the dry residue the extract is obtained. It contains 10-50 ug/g of L-alanine. Density of the extract: 0,99 ÷ 1.01 g/ml. The roots from the cultivated or wild plant collected in Poland, Hungary and Serbia are harvested during autumn, winter and spring and are dried at 35-40° C and stored protected from light untill processed.

$$\begin{array}{ccc} c & B & G \\ \hline & M & E & B \end{array}$$

Mixtures.....???

Thank you for your attention