

HERBAL MEDICINES

Naming and records

Ciska Matai, CBG-MEB

September 2013

COLLEGE
TER BEOORDELING VAN
GENEESMIDDELEN

C B G

M E B

MEDICINES
EVALUATION
BOARD

Definition Herbal medicinal products

Directive 2001/83/EC and Directive 2004/24/EC

- Herbal medicinal product:

Any medicinal product, exclusively containing as active ingredients 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;

- Herbal preparations:

Preparations obtained by subjecting herbal substances to treatments such as extraction, distillation, expression, fractionation, purification, concentration or fermentation. These include comminuted or powdered herbal substances, tinctures, extracts, essential oils, expressed juices and processed exudates.

- Herbal substances:

All mainly whole, fragmented or cut plants, plant parts, algae, fungi, lichen in an unprocessed, usually dried, form, but sometimes fresh. Certain exudates that have not been subjected to a specific treatment are also considered to be herbal substances. Herbal substances are precisely defined by the plant part used and the botanical name according to the binomial system (genus, species, variety and author)

Quality requirements and naming of Herbal substances

- The quality of herbal medicinal products is determined by the quality of the starting plant material, in-process controls, GMP controls, process validation and by specifications applied to them throughout development and manufacture.
- Consistent quality of products of herbal origin can only be assured if the starting plant material is defined in a rigorous and detailed manner, particularly the specific botanical identification of the plant material used. It is also important to know the geographical source and the conditions under which the herbal substance is obtained in order to ensure that the material is of consistent quality.

Quality requirements and naming of Herbal substances

- The 'Guideline on Good Agricultural and Collection Practice for starting materials of herbal origin' provides recommendations for an appropriate quality assurance system on the cultivation and harvesting of plant materials.
- In addition, in accordance with European medicines legislation, the quality dossier should address potential contamination by micro-organisms, products of micro-organisms, pesticides, toxic metals, radioactive contamination, fumigants, etc. Thus, the potential for residues of fumigation agents should be fully considered.

Guideline on Quality of Herbal Medicinal Products/
Traditional Herbal Medicinal Products.

CPMP/QWP/2819/00 Rev 1, EMEA/CVMP/814/00 Rev 1

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

- All herbal substances/herbal preparations are essentially defined by their production process and their specifications;
- Standardized herbal substances/herbal preparations are adjusted to a given content of constituents with known therapeutic activity within an acceptable tolerance; standardization is achieved by adjustment of the herbal substances/herbal preparations with excipients or by blending batches of herbal substances and/or herbal preparations;
- 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;
- 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.

Herbal substances and herbal preparations consisting of comminuted or powdered herbal substances

EXAMPLES

- Active substance

Name: Sennae folium

Quantity: 415-500 mg, corresponding to 12.5 mg of hydroxyanthracene glycosides, calculated as Sennoside B.

- Active substance

Name: Salicis cortex

Quantity: 4 g, corresponding to 40 to 48 mg of total phenolic glycosides, expressed as salicin.

- Active Substance

Name: Valerianae radix 900 mg

Naming of Herbal substances in SmPC section 2

5. Declaration of herbal substances in the SmPC

The declaration of a herbal substance should cover the name and the quantity of the herbal substance. The name of the herbal substance is the scientific Latin name of the plant species according to the binomial system (genus, species, variety and author) with the Latin term of the plant part, followed by the [translated] common name of the monograph of the European Pharmacopoeia if available, or else of the Pharmacopoeia of a Member State, if available, or else the common name of the herbal substance (in brackets).

The following characteristics have to be stated in the declaration:

1. Name of the herbal substance.
2. Quantity of the genuine herbal substance.
3. Name and quantity of the constituent(s) with known therapeutic activity (standardised herbal substances), if applicable.
4. Name and quantity (given as a range) of the active markers (quantified herbal substances), if applicable.

673 - HARPAGOPHYTI RADIX, DROOG EXTRACT, ETHANOL-WATER 60 pCt. (1,5-3,0 = 1)

Property	Value
CBG Number:	673
CAS Number:	
* Dutch Name:	HARPAGOPHYTI RADIX, DROOG EXTRACT, ETHANOL-WATER 60 pCt. (1,5-3,0 = 1)
Active Ingredient Synonym:	"Dry ethanolic-water 60 pCt. extract obtained from Devil's claw secondary roots."; "Devil's claw root consists of the cut and dried, tuberous secondary roots of Harpagophytum procumbens DC. and/or Harpagophytum zeyheri Decne."; "Droog ethanol-water 60 pCt. extract van de Duivelsklauwwortel (H.zeyheri Decne en/of H. procumbens D.C.)"; "Droog extract van Windhoek-plantwortel"; "Droog extract van Namibië-plantwortel"
Origin:	
Latin Name:	HARPAGOPHYTI EXTRACTUM SICCUUM
INN Name:	HARPAGOPHYTI RADIX, DRY EXTRACT
English Name:	DEVIL'S CLAW DRY EXTRACT, ETHANOL-WATER 60pCt (1,5-3,0 = 1)
Inactive Ingredient Name:	
Notes:	Devil's claw root consists of the cut and dried, tuberous secondary roots of Harpagophytum procumbens DC. and/or Harpagophytum zeyheri Decne. Content: minimum 1.2 per cent of harpagoside (C ₂₄ H ₃₀ O ₁₁ ; Mr 494.5) (dried drug). Devil's claw root the characteristic constituents are: Iridoid glucosides, principally harpagoside together with small amounts of harpagide, 8-pcoumaroylharpagide, procumbide and its 6'-p-coumaroyl ester. The phenolic glycosides acteoside (verbascoside) and isoacteoside, and sugars, mainly the tetrasaccharide stachyose with smaller amounts of raffinose, sucrose and monosaccharides are also present. Harpagoside is used as quality marker for both the herbal substance and the herbal preparation. Manufacture: Macerate the roots with 60 pCt. ethanol-water. The macerate is pressed/decanted from the tincture and waisted. The tincture is heated and concentrated and lactose is added. After drying and milling the final extract is achieved.

DEVIL'S CLAW ROOT

Harpagophyti radix

DEFINITION

Cut and dried, tuberous secondary roots of *Harpagophytum procumbens* DC. and/or *Harpagophytum zeyheri* Decne.

Content: minimum 1.2 per cent of harpagoside ($C_{24}H_{30}O_{11}$; M_r 494.5) (dried drug).

IDENTIFICATION

- A. It consists of thick, fan-shaped or rounded slices or of roughly crushed discs. The darker outer surface is traversed by tortuous longitudinal wrinkles. The paler cut surface shows a dark cambial zone and xylem bundles distinctly aligned in radial rows. The central cylinder shows fine concentric striations. Seen under a lens, the cut surface presents yellow or brownish-red granules.

01/2008:1871

DEVIL'S CLAW DRY EXTRACT

Harpagophyti extractum siccum

DEFINITION

Dry extract obtained from [Devil's claw root \(1095\)](#).

Content: minimum 1.5 per cent of harpagoside ($C_{24}H_{30}O_{11}$; M_r 494.5) (dried extract).

PRODUCTION

The extract is produced from the herbal drug by an appropriate procedure using either water or a hydroalcoholic solvent that is at most equivalent in strength to ethanol (95 per cent V/V).

Information from the Registration Dossier

3.2.S.1.1 Nomenclature

Definition of the herbal substance:

Binomial scientific name of the plant:	<i>Harpagophytum procumbens</i> D.C. and/or <i>H. zeyheri</i> L. Decne.
Scientific name of plant:	<i>Harpagophytum procumbens</i> D.C. and/or <i>H. zeyheri</i> L. Decne.
Synonyms:	Radix <i>harpagophyti</i> , tubera <i>harpagophyti</i>
German name:	Teufelskrallenwurzel
English name:	Devils` claw root
Parts of the plant:	The dried secondary roots of <i>harpagophytum procumbens</i> D.C. and/or <i>H. zeyheri</i> L. Decne.

Definition of the herbal preparation:

- Definition of the herbal preparation: Harpagophyti extractum
- Ratio of the herbal substance to the herbal preparation: DER_{native} 1.5 - 3 : 1 referred to the dried drug
- Extraction solvent: Ethanolum 60 % (V/V)

Laboratory code: corresponds Art. No.: 01308200

Information from the Registration Dossier

3.2.S.1.2 Structure

Constituents of the herbal substance:

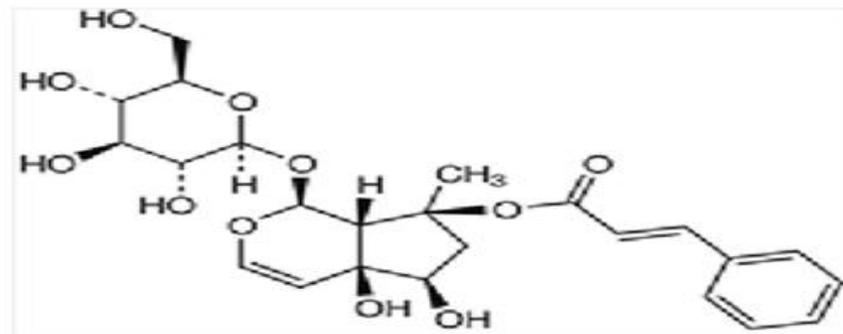
According to ESCOP monograph on Devil's claw root the characteristic constituents are:

Iridoid glucosides, principally harpagoside together with small amounts of harpagide, 8-*p*-coumaroylharpagide, procumbide and its 6'-*p*-coumaroyl ester. The phenolic glycosides acteoside (verbascoside) and isoacteoside, and sugars, mainly the tetrasaccharide stachyose with smaller amounts of raffinose, sucrose and monosaccharides are also present.

Physical form of the herbal preparation:

The herbal preparation (drug substance) is a fine and hygroscopic powder.

For quantitative determinations (evidence of batch to batch conformity) the marker used is harpagoside (in the herbal substance and in the herbal preparation as well as in the herbal product).|



Chemical Structure of Harpagoside

Information from the Registration Dossier

Description of the herbal substance: Harpagophyti radix

According to Ph.Eur.:

Devil's claw root consists of the cut and dried tuberous, secondary roots of *Harpagophytum procumbens* D.C., and/or *H. zeyheri* L. Decne.

It consists of thick, fan-shaped or rounded slices or of roughly crushed discs. The darker outer surface is traversed by tortuous longitudinal wrinkles. The paler cut surface shows a dark cambial zone and xylem bundles distinctly aligned in radial rows. The central cylinder shows fine concentric striations. Seen under a lens, the cut surface presents yellow to brownish-red granules.

Description of the herbal preparation: Harpagophyti extractum

The herbal preparation (drug substance) is a brownish yellow, fine and hygroscopic powder with a light to dark brown colour, odourless and has a bitter taste.

SmPC section 2

2 Kwalitatieve en kwantitatieve samenstelling

Een filmomhulde tablet (\approx 855 mg) bevat:

480 mg extract (als droogextract) van *Harpagophytum procumbens* DC. en/of *Harpagophytum zeyheri* Decne, radix (Duivelsklauwwortel), overeenkomend met 720 - 1440 mg gedroogde wortels.

Extractiemiddel: ethanol 60% (v/v)

Close

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:	MARSHMALLOW ROOT EXTRACT
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.

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 un lignified, 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.

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

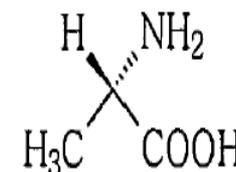
Extract of marshmallow root (1 : 19.5 - 23.5) is a clear to light cloudy yellowish liquid with a faint fruity odor. It contains 10 - 50 µg/g of L-alanine.

German name: L-Alanin

Structure:

English name: L-alanine

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



Synonyms: α-aminopropionic acid

Sum formula: C₃H₇NO₂

Substance class: Amino acid

CAS No.: 56-41-7

Molecular weight: 89.1 g/mol

Characteristics: white, crystalline powder or colorless, orthorhombic crystals, soluble in water, poorly soluble in alcohol, insoluble in diethyl ether.

Melting point: 297 °C (disintegration)

Information from the Registration Dossier

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.

$\frac{c \ B \ G}{M \ E \ B}$



THANK YOU FOR YOUR ATTENTION