



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

12 July 2011
EMA/HMPC/262767/2010
Committee on Herbal Medicinal Products (HMPC)

Assessment report on *Capsella bursa-pastoris* (L.) Medikus, herba

Based on Article 16d(1), Article 16f and Article 16h of Directive 2001/83/EC as amended (traditional use)

Final

Herbal substance(s) (binomial scientific name of the plant, including plant part)	<i>Capsella bursa-pastoris</i> (L.) Medikus, herba
Herbal preparation(s)	Comminuted herbal substance Liquid extract (DER 1:1), extraction solvent ethanol 25% V/V
Pharmaceutical forms	Comminuted herbal substance as herbal tea for oral use. Herbal preparations in liquid dosage forms for oral use.
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1. Introduction

1.1. Description of the herbal substance(s), herbal preparation(s) or combinations thereof

- Herbal substance(s)

Capsella bursa-pastoris (Fam. *Brassicaceae/Cruciferae*) is a common cosmopolitan weed growing up to 40 cm and indigenous to Europe, West Africa and Asia. The Latin and common names are derived from the (shepherd's) purse shape of the plant's seed pods. Common names are: shepherd's purse (English), bourse à pasteur (French), herderstasje (Dutch), Hirtentäschelkraut (German), bolsa de pastor (Spanish). Common names in the other EU official languages can be found in the monograph.

For *Capsella herba* there is no Ph. Eur. monograph available. Therefore the monographs of the British Herbal Pharmacopoeia 1996 (BHP), the French Pharmacopoeia (Ph. Fr.) and the Complete German Commission E (Blumenthal, 1998) have been consulted.

The BHP monograph describes *Capsella* as the dried, aerial parts of *Capsella bursa-pastoris* (L.) Medikus and includes macroscopic and microscopic characteristics (including weak, rather unpleasant odour and slightly saline and astringent taste) (BHP, 1996).

The description in the French Pharmacopoeia is: «La partie utilisée de la bourse à pasteur est constituée par les parties aériennes fleuries et fructifères, séchées de *Capsella bursa-pastoris* (L.) Medikus récoltées en fin de floraison et en cours de fructification» (Fr. Ph., 1997).

Capsella herba (*Bursae pastoris herba*) consists of the fresh or dried, above-ground parts of *Capsella bursa-pastoris* (L.) Medikus (synonym: *Thlaspi bursa-pastoris* L.) as well as its preparations in effective dosage (Blumenthal, 1998).

There is no monograph for *Capsella herba* included in the WHO monographs on selected medicinal plants.

Constituents (Felter, 1922 ; BHP, 1983 ; van Hellemont, 1988; Maillard *et al.*, 1988; Wichtl, 1994; Khare, 2007; Barnes *et al.*, 2007; Song *et al.*, 2007):

- Flavonoids (a.o. flavonglycosides): quercetin, tricetin, diosmetin, kaempferol, luteolin, hesperitin and derivated glycosides (e.g. rutin, diosmin, hesperidin, luteolin-7-rutinoside, luteolin-7-galactoside, quercetin-3-rutinoside).
- Amines: choline (1%) , acetylcholine, histamine
- Aminoacids (22, a.o. proline, tyramine, and ornithine), (poly)peptides (a.o. α - and γ -aminobutyric acid, α -aminoadipic acid) and proteins
- Aliphatic and phenolic acids: chlorogenic, vanilic, syringic, fumaric acid
- Volatile oil, with at least 74 components identified, with camphor as major constituent (0.02%)
- Resin
- Saponins
- Other constituents: 9-methylsulfinylnonyl and 10-methylsulfinyldecyl glucosinolates (in seeds), carotenoids, ascorbic acid, vitamin K, cardenolide, calcium and potassium salts, unidentified alkaloids, mustard oil glucoside (e.g. sinigrin, possibly responsible for the off-flavours in dairy products,). Examination of annual crucifers revealed that the concentration of sinigrin in

Capsella bursa-pastoris is lower than that of mustard oil glycosides in other cruciferous plants (Park, 1967). See also 3.3 Overview of available toxicological data.

From a study on the nutritional composition of wild edible crucifer species, a relatively high quantity of fatty acids ω 6-polyunsaturated fatty acids was found in *Capsella*. The amount of erudic acid (C22:1 ω 9), a fatty acid present in plant oils of species of Crucifera, known as toxic acid involved in the development of myocarditis, appeared to be very low (Guil-Guerrero *et al.*, 1999).

In a joint study of Universities of Jordan and Pakistan, results of chemical analysis of aerial parts of *Capsella bursa-pastoris* revealed the components cupressoflavone (in chloroform phase) and swertisin (in aqueous phase) (Al-Khalil *et al.*, 2000).

A benzene extract of the aerial parts of *Capsella bursa-pastoris* was fractionated into seven fractions: polar lipids (34.7%), free fatty acids, triterpenols (25.8%), diacylglycerols, waxy esters (12.8%), sterols, chlorophylls (12.4%), triacylglycerols (6.7%), unidentified compounds (4.1%) and hydrocarbons (3.5%) (Bekker *et al.*, 2002).

A quaternary ammonium salt has been isolated from the herb which is reported to be responsible for its activity (Kuroda 1968; Khare, 2007).

Young leaves contain Vitamin A (5,000 IU/100 g) and ascorbic acid (91 mg/100 g) (Khare, 2007).

Relatively high quantities of minerals in *Capsella* have been reported, however a low percentage of Na content (Guil-Guerrero *et al.*, 1999).

Analysis of herbs and their decoctions and tinctures by Inductively Couple Plasma Optical Emission Spectroscopy revealed that *Capsella* contains essential elements as Ca, Cu, Cr, Fe, K, Mg, Mn, Na and Zn, of which some in relatively high amounts (Ca, Cr, K and Na) compared to the other 9 analysed plant species (Szentmihalyi *et al.*, 2005).

Capsella appeared to be a potential useful biomonitor of the four heavy metals studied (Pb, Cd, Zn and Cu) for monitoring polluted urban areas (Aksoy, 1999).

Assessor's comment:

Data on the cardenolide and sinigrin content of *Capsella bursa-pastoris* is lacking.

- *Combinations of herbal substance(s) and/or herbal preparation(s)*

BHP (1983) mentions the combined use with *Trillium* and *Hydrastis* in menorrhagia or metrorrhagia and combined use with *Agothosma* in cystitis. In BHP (1996), only the anti-haemorrhagic action is mentioned.

Capsella herba is used in combinations with many other herbal substances / herbal preparations, mainly to be used as infusion. Combinations with other herbs have been mentioned in teas to be used for symptoms in cardiovascular conditions (Wichtl, 1994).

Capsella is marketed in combination with other herbs (e.g. *Achillea*, *Majorana* and *Quercus*) in health products to regulate menstruation and in urological products (drops and tablets) (Wichtl, 1994).

In Canada, *Capsella* is an approved active ingredient in nearly 20 Schedule OTC Traditional Herbal Medicines (Wichtl, 1994).

Actual market information on *Capsella* containing medicinal products with a marketing authorisation or registration is given in the next section.

The monograph exclusively refers to *Capsella herba*.

1.2. Information about products on the market in the Member States

Capsella herba in medicinal products

From the requests for information to all Member States, most agencies responded that there are no authorised or registered medicinal products containing Capsella on their market. Germany reported two Marketing Authorisations for herbal teas with Capsella as single active ingredient and in both Germany and Hungary Capsella is on the market in combination products to be used for tea preparation (Traditional Use). See also **Regulatory Status Overview**.

Country	Product information	Therapeutic indication	Dosage	On market since
Germany	WEU: 2 Standard Marketing Authorisations for herbal teas with Capsella as single active ingredient TU: 1 combination product for tea preparation	Symptomatic treatment of mild menorrhagia and metrorrhagia (conform Commission E)		
Hungary	Herbal tea: per sachet: 0.210 g Matricaria flos, 0.175 g Millefoli herba, 0.175 g Bursae pastoris herba, 0.140 g Foeniculi dulcis fructis	Symptoms prior to menstruation; due to its components having spasmolytic, antiphlogistic and anti-dyspeptic effects, the herbal tea relieves the sensation of bloating	Starting 3-5 days before the menstruation and should be applied during the whole menstrual cycle. 3-5x2-3 sachets as an infusion prepared with 3-5 dl hot water (infusion time: 5-10 minutes)	23-03-2006

There are many Capsella containing preparations on the market as (un)licensed health products under Food Law. For these preparations no published data has been documented, which could be supportive evidence on tradition, indication or posology.

A single-ingredient preparation Styptysat[®], a dry extract (4.1:1; solvent water) of Capsella herba, is on the market in Germany (Wichtl, 1994; Martindale, 2009).

Fenneherb Cystaid[®] is another multi-ingredient preparation on the UK market (Barnes *et al.*, 2007).

Martindale includes references to proprietary products:

Austria: Menodoron;

France: Hemoluol¹, Histo-Fluine P, Tisane Provençale no 3, Tisanes de l'Abbé Hamon no 14

Germany: Bilisan forte, Bomagall forteS, Dr. Klingers Bergischer Krautertee, Leber-und Gallentee, Duoform, Gallitophen, Menodoron, Menstrualin, Original-Hico-Gallenheil, Presselin Dysmen Olin 3 N, Rhoival, Rowaclimax

Poland: Klimax, Prostapol, Uroprost

Spain: Proctosor

United Kingdom: Antitis, Sciargo (Martindale, 2009).

Regulatory status overview

Member State	Regulatory Status				Comments
Austria	<input type="checkbox"/> MA	<input type="checkbox"/> TRAD	<input type="checkbox"/> Other TRAD	<input type="checkbox"/> Other Specify:	No medicinal products on market with Capsella
Belgium	<input type="checkbox"/> MA	<input type="checkbox"/> TRAD	<input type="checkbox"/> Other TRAD	<input type="checkbox"/> Other Specify:	
Bulgaria	<input type="checkbox"/> MA	<input type="checkbox"/> TRAD	<input type="checkbox"/> Other TRAD	<input type="checkbox"/> Other Specify:	No products with MA; no info on food supplements
Cyprus	<input type="checkbox"/> MA	<input type="checkbox"/> TRAD	<input type="checkbox"/> Other TRAD	<input type="checkbox"/> Other Specify:	
Czech Republic	<input type="checkbox"/> MA	<input type="checkbox"/> TRAD	<input type="checkbox"/> Other TRAD	<input type="checkbox"/> Other Specify:	
Denmark	<input type="checkbox"/> MA	<input type="checkbox"/> TRAD	<input type="checkbox"/> Other TRAD	<input type="checkbox"/> Other Specify:	No medicinal products on market with Capsella
Estonia	<input type="checkbox"/> MA	<input type="checkbox"/> TRAD	<input type="checkbox"/> Other TRAD	<input type="checkbox"/> Other Specify:	No medicinal products on market with Capsella
Finland	<input type="checkbox"/> MA	<input type="checkbox"/> TRAD	<input type="checkbox"/> Other TRAD	<input type="checkbox"/> Other Specify:	
France	<input type="checkbox"/> MA	<input type="checkbox"/> TRAD	<input type="checkbox"/> Other TRAD	<input type="checkbox"/> Other Specify:	Only in combn products (2 WEU-products containing herbals + chemical component; 1 TU - product containing only herbals)
Germany	<input checked="" type="checkbox"/> MA	<input type="checkbox"/> TRAD	<input type="checkbox"/> Other TRAD	<input type="checkbox"/> Other Specify:	WEU: 2 herbal teas with Capsella as single ingredient TU: 1 combination product for tea preparation
Greece	<input type="checkbox"/> MA	<input type="checkbox"/> TRAD	<input type="checkbox"/> Other TRAD	<input type="checkbox"/> Other Specify:	
Hungary	<input type="checkbox"/> MA	<input type="checkbox"/> TRAD	<input type="checkbox"/> Other TRAD	<input type="checkbox"/> Other Specify:	1 combination product for tea preparation as THMP, 1 herbal tea with Capsella as single ingredient on market as food
Iceland	<input type="checkbox"/> MA	<input type="checkbox"/> TRAD	<input type="checkbox"/> Other TRAD	<input type="checkbox"/> Other Specify:	
Ireland	<input type="checkbox"/> MA	<input type="checkbox"/> TRAD	<input type="checkbox"/> Other TRAD	<input type="checkbox"/> Other Specify:	

¹ This preparation is discontinued or no longer marketed

Member State	Regulatory Status				Comments
Italy	<input type="checkbox"/> MA	<input type="checkbox"/> TRAD	<input type="checkbox"/> Other TRAD	<input type="checkbox"/> Other Specify:	
Latvia	<input type="checkbox"/> MA	<input type="checkbox"/> TRAD	<input type="checkbox"/> Other TRAD	<input type="checkbox"/> Other Specify:	No medicinal products on market with Capsella
Liechtenstein	<input type="checkbox"/> MA	<input type="checkbox"/> TRAD	<input type="checkbox"/> Other TRAD	<input type="checkbox"/> Other Specify:	
Lithuania	<input type="checkbox"/> MA	<input type="checkbox"/> TRAD	<input type="checkbox"/> Other TRAD	<input type="checkbox"/> Other Specify:	
Luxemburg	<input type="checkbox"/> MA	<input type="checkbox"/> TRAD	<input type="checkbox"/> Other TRAD	<input type="checkbox"/> Other Specify:	
Malta	<input type="checkbox"/> MA	<input type="checkbox"/> TRAD	<input type="checkbox"/> Other TRAD	<input type="checkbox"/> Other Specify:	
The Netherlands	<input type="checkbox"/> MA	<input type="checkbox"/> TRAD	<input type="checkbox"/> Other TRAD	<input type="checkbox"/> Other Specify:	No medicinal products on market with Capsella
Norway	<input type="checkbox"/> MA	<input type="checkbox"/> TRAD	<input type="checkbox"/> Other TRAD	<input type="checkbox"/> Other Specify:	
Poland	<input type="checkbox"/> MA	<input type="checkbox"/> TRAD	<input type="checkbox"/> Other TRAD	<input type="checkbox"/> Other Specify:	
Portugal	<input type="checkbox"/> MA	<input type="checkbox"/> TRAD	<input type="checkbox"/> Other TRAD	<input type="checkbox"/> Other Specify:	
Romania	<input type="checkbox"/> MA	<input type="checkbox"/> TRAD	<input type="checkbox"/> Other TRAD	<input type="checkbox"/> Other Specify:	
Slovak Republic	<input type="checkbox"/> MA	<input type="checkbox"/> TRAD	<input type="checkbox"/> Other TRAD	<input type="checkbox"/> Other Specify:	No medicinal products on market with Capsella
Slovenia	<input type="checkbox"/> MA	<input type="checkbox"/> TRAD	<input type="checkbox"/> Other TRAD	<input type="checkbox"/> Other Specify:	
Spain	<input type="checkbox"/> MA	<input checked="" type="checkbox"/> TRAD	<input type="checkbox"/> Other TRAD	<input type="checkbox"/> Other Specify:	Only in combination products
Sweden	<input type="checkbox"/> MA	<input type="checkbox"/> TRAD	<input type="checkbox"/> Other TRAD	<input type="checkbox"/> Other Specify:	
United Kingdom	<input type="checkbox"/> MA	<input checked="" type="checkbox"/> TRAD	<input type="checkbox"/> Other TRAD	<input type="checkbox"/> Other Specify:	Only in combination products

MA: Marketing Authorisation

TRAD: Traditional Use Registration

Other TRAD: Other national Traditional systems of registration

Other: If known, it should be specified or otherwise add 'Not Known'

This regulatory overview is not legally binding and does not necessarily reflect the legal status of the products in the MSs concerned.

1.3. Search and assessment methodology

Not specified by the Rapporteur.

2. Historical data on medicinal use

2.1. Information on period of medicinal use in the Community

European tradition

Steinmetz (1954) mentions that an infusion of Capsella is cooling, diuretic and astringent and therefore beneficial in all kinds of blood and bladder problems (diarrhoea with sharp and bloody stools, piles, profuse menses, dropsy, diseases of bladder, spitting of blood). *Extractum Capsellae Bursae pastoris liquidum* is used as a substitute for ergot of rye to arrest bleeding from lungs, stomach, uterus and kidneys. Steinmetz addresses the considerable haemostatic action to the fungi *Cystopus Candidus* and *Peronospora Grisea*, which would grow on the plant and produce the odour of trimethylamine. Also Wichtl (1994) mentions the former common use of Capsella as a substitute for ergot in uterine

haemorrhaging, and its continuous use in folk medicine to treat dysmenorrhoea. Van Hellemont states that both ergot and Capsella are useful in meno- and metrorrhagia, but ergot would perform a stronger haemostyptic activity (van Hellemont, 1988).

According to Wichtl (1994), Capsella is still occasionally used in traditional medicine as a styptic remedy (its former common use as a substitute for ergot in uterine haemorrhaging is obsolete). It is used in European traditional medicine for preventing or arresting haemorrhage, more specifically to treat dysmenorrhoea.

Asian tradition

In Tibetan medicine, Capsella is used to stop vomiting, to treat kidneys, lungs and nerve disorders and fluid retention of the body (Wichtl, 1994). Capsella is used in Indian medicine in menorrhagia and haemorrhages from renal and genito-urinary tract, in diarrhoea and dysentery and as a diuretic (Khare, 2007).

In China, a decoction of the whole plant is used in hypertension and as haemostatic agent for treatment of chyluria (fat globules in the urine) and hematuria (Herbalgram, 2008).

2.2. Information on traditional/current indications and specified substances/preparations

The following indications have been reported for *Capsella bursa pastoris*:

Blood/Haemorrhages/Bleeding

reference	indication	preparation
Felter, 1922	Passive haemorrhages (and slight stimulant in amenorrhoea)	- Specific Medicine Capsella Infusum Capsella
Steinmetz, 1954	Haemostatic agent for all kind of bleedings	- Infusion - Extractum <i>Capsella Bursae pastoris</i> liquidum
BHP, 1983	Anti-hemorrhagic	- Infusion - Liquid Extract (1:1 in 25% alcohol)
van Hellemont, 1988	Blood pressure lowering	- Herba bursae pastoris as infusion - Extractum bursae pastoris - Tinctura bursae pastoris Rademacher - Capsella bursae pastoris Mother Tincture (M.T.(ø)) - Extractum fluidum bursae pastoris
van Hellemont, 1988	Bleeding wounds (topical use)	Ointment or tincture
Blumenthal, 1998	Nosebleeds and superficial bleeding skin injuries (local/external application)	- Infusion - Fluidextract (acc. to Erg. B. 6)

KNMP, 1990	Haemostatic agent (menstrual and nose bleedings)	- Infusion - Thlaspi bursae-pastoris \emptyset (1:2 fresh whole plant in 50% alcohol V/V)
Wichtl, 1994	As haemostatic agent	- Infusion - Dry extract (DER 4.1:1; solvent water)
Barnes <i>et al.</i> , 2007	Anti-hemorrhagic (traditionally used for haematemesis, hematuria)	- Infusion - Liquid extract (1:1 in 25% alcohol)

Menorrhagia / Metrorrhagia

reference	indication	preparation
Felter, 1922	Prolonged and oft-occurring menorrhagia with too long, too frequent, almost colourless flow	- Specific Medicine Capsella Infusum Capsella
Steinmetz, 1954	Profuse menses	- Infusion - Extractum Capsella Bursae pastoris liquidum
BHP 1983	Uterine haemorrhage, menorrhagia, hematestatis, hematuria, (in combination with Trillium and Hydrastis)	- Infusion - Liquid Extract (1:1 in 25% alcohol)
van Hellemont, 1988	Hemostypticum in menorrhagia and metrorrhagia	- Herba bursae pastoris as infusion - Extractum bursae pastoris - Tinctura bursae pastoris Rademacher - Capsella bursae pastoris M.T.(\emptyset) - Extractum fluidum bursae pastoris
Wichtl, 1994	Dysmenorrhea	- Infusion - Dry extract (DER 4.1:1; solvent water)
Mc Guffin <i>et al.</i> , 1997	As emmenagogue/uterine stimulant	
Blumenthal, 1998; Schulz <i>et al.</i> , 1998	Symptomatic treatment of mild menorrhagia and metrorrhagia	- Infusion - Fluidextract (acc. to Erg. B. 6)
Barnes <i>et al.</i> , 2007	Menorrhagia	- Infusion - Liquid extract (1:1 in 25% alcohol)

Khare, 2007	Menorrhagia	- Juice extracts
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Urinary tract and intestines

reference	indication	preparation
Felter, 1922	Irritation of urinary organs with phosphatic deposits, atonic disorders with constant desire to urinate	- Specific Medicine Capsella Infusum Capsella
Steinmetz, 1954		- Infusion - Extractum Capsella Bursae pastoris liquidum
BHP, 1983	(Acute catarrhal) cystitis, as urinary antiseptic (in combination with Agathosma)	- Infusion - Liquid Extract (1:1 in 25% alcohol)
Barnes <i>et al.</i> , 2007	Urinary antiseptic, diarrhoea and acute catarrhal cystitis	- Infusion - Liquid extract (1:1 in 25% alcohol)
Khare, 2007	Haemorrhages from renal and genito-urinary tract, diarrhoea and dysentery	- Juice extracts

Documented medicinal uses:

Based on above mentioned references Capsella herba is considered to be a traditional herbal medicinal product for use in the specified indications exclusively based upon long-standing use:

- as anti-haemorrhagic in all kinds of bleedings, including skin injuries and nosebleeds (oral and topical use)
- for symptomatic treatment of mild menorrhagia and metrorrhagia

Assessor's comment:

Due to the lack of sufficient data to support the traditional use (i.e. no information on the extent and duration of use and/or defined posology) as antiseptic agent in diarrhoea and cystitis and as blood pressure lowering agent, these uses have not been included into the monograph.

The treatment of nosebleed and bleeding due to skin injuries is also not included in the monograph because for these indications a tea preparation is used. The tea preparation and the cooling of the tea would take at least 30 minutes. During this time, bleeding should already have stopped.

2.3. Specified strength/posology/route of administration/duration of use for relevant preparations and indications

Posology for adolescents and adults

Herbal substance and comminuted herbal substance for tea preparation *for oral use*

reference	single dose per 150 ml of water	daily dose	indication
BHP, 1983; Barnes <i>et al.</i> , 2007	1-4 g	3-12 g	Menorrhagia, haematemesis, haematuria, uterine haemorrhage, diarrhoea and acute catarrhal cystitis
van Hellemont, 1988	5 g	10-20 g	Hemostypticum in menorrhagia and metrorrhagia; blood pressure lowering
KNMP, 1990	2.5-5g	5-20 g	Haemostatic agent (menstrual and nose bleedings)
Wichtl, 1994	3-5 g	up to 15 g	As haemostatic agent, dysmenorrhoea
Blumenthal, 1998		10-15 g equivalent preparations	Symptomatic treatment of mild menorrhagia and metrorrhagia
Schulz <i>et al.</i> , 1998		5-15 g	Symptomatic treatment of mild menorrhagia and metrorrhagia

Herbal substance and comminuted herbal substance for preparation of infusion *for topical use (poultice or nasal dressing)*

reference	single dose per 150 ml of water	daily dose	indication
Wichtl , 1994; Blumenthal, 1998	3-5 g per $\frac{3}{4}$ of water	dose freely	As haemostatic agent; nosebleeds and superficial bleeding skin injuries

Herbal preparation: Liquid extract (1:1 in 25% alcohol) *for oral use*

reference	single dose	daily dose	indication
BHP, 1983; Barnes <i>et al.</i> , 2007	1-4 ml	3-12 ml	Menorrhagia, haematemesis, haematuria, diarrhoea and acute catarrhal cystitis

Herbal preparation: Liquid extract (acc. to Erg. B. 6)² *for oral use*

reference	single dose	daily dose	indication
Wichtl, 1994; Blumenthal, 1998		5-8 g	Symptomatic treatment of mild menorrhagia and metrorrhagia, as haemostatic agent, dysmenorrhoea

Herbal preparation: Liquid extract (acc. to Erg. B. 6) *for topical use*

reference	single dose	daily dose	indication
Blumenthal, 1998; Herbalgram, 2008		5-8 g	nosebleeds and superficial skin wounds and bruising

Posology for children (information from: 'Heilpflanzen in der Kinderheilkunde' (Bühning *et al.*, 2007)

Herbal substance and comminuted herbal substance for tea preparation *for oral use*

age in years	daily dose
0-1	-
1-4	-
4-10	-
10-16	10-15 g

Herbal substance and comminuted herbal substance for preparation of infusion *for topical use (poultice or nasal dressing)*

age in years	daily dose
0-1	-
1-4	2-3.5 g/150 ml
4-10	2-3.5 g/150 ml
10-16	3-5 g/150 ml

² Ergänzungsbuch zum DAB 6 (1941)

Assessor's comment:

There is no indication for the use of Capsella in children for menstrual bleeding; other uses of Capsella described in Bühring *et al.* 2007 for children from 0 to 16 years of age are: superficial bleeding skin injuries, gum bleeding and nosebleeds. The use of Capsella in children is described only in this reference, the duration of experience with medicinal use in children is unknown. Furthermore, (non-)clinical data to support the safe use in children are lacking. Therefore, the use in children is not included in the monograph.

The use of Capsella for menstrual bleeding in adolescents under 18 years of age is not recommended because of concerns requiring medical advice.

Other preparations

In the consulted documentation, the following preparations have been mentioned, but due to lack of information (either the herbal preparation is not clearly specified and/or the posology has not been documented), these cannot be included into the monograph.

preparation	single dose	daily dose	reference
Acidum bursanicum			Bombelon, 1888 (in Kuroda 1969)
Specific Medicine Capsella	1-60 drops		Felter, 1922
Infusion (of fresh herb)		dosing freely	Felter, 1922
Extractum Capsella Bursae pastoris liquidum			Steinmetz, 1954
Extractum bursa-pastoris	2 g	2-3 times daily	van Hellemont, 1988
Tinctura bursa-pastoris Rademacher (from fresh herb)	20-40 drops	several times daily	van Hellemont, 1988
Extractum fluidum bursa-pastoris	5-15 g daily or 1 teaspoon	2-4 times daily	van Hellemont, 1988
Thlaspi bursa-pastoris ø (1:2 fresh whole plant in 50% alcohol V/V)			KNMP, 1990
Dry extract (DER 4.1: 1; water)			Wichtl, 1994
Juice extracts			Barnes <i>et al.</i> , 2007; Khare, 2007

Summary

Oral administration and topical application are the routes of administration for Capsella herba preparations in the recommended traditional indications. From the information found in the handbooks, the posology data for the specified preparations can be summarised as follows.

Posology for adults (oral use)

Indication: symptomatic treatment in menorrhagia and metrorrhagia

	single dose	daily dose
A) Herbal substance and comminuted herbal substance for tea preparation	1-5 g	3-20 g
B) Liquid extract 1:1 in 25% alcohol	1-4 ml	3-12 ml
C) Liquid extract (acc. to Erg. B. 6)		5-8 g

Assessor's comment:

No restriction on the duration of use has been reported for Capsella herba.

If the symptoms persist during the use of the medicinal product, a doctor or a qualified health care practitioner should be consulted.

2.4. Assessor's overall conclusion on the historical data on medicinal use

Historical data on the medicinal use of Capsella herba is predominantly based on the use of Capsella herb as infusion, to a lesser extent to other preparations. Of all mentioned preparations, few are well specified and defined with data on posology. For acceptance in the monograph, the traditional use of the individual preparations based on Capsella has been evaluated:

- The use of Capsella herba *as an infusion* for the treatment of haemorrhages has been reported at least since 1922 and can be accepted according to the requirement for 30 years of medicinal use in Europe. Many handbooks have published information on the use of this infusion, including dosages for both oral and topical application. In Germany Capsella herbal substance is still on the market both as a single ingredient and in combination products for tea preparation.
- The use of Capsella herba *liquid extract (1:1 in 25% alcohol)* for the treatment of haemorrhages/bleedings has been reported at least since 1983 and can therefore be accepted according to the requirement for 30 years of medicinal use in Europe. Several handbooks mention the use and dosage of this liquid extract, therefore this extract can be included into the monograph.
- The use of Capsella herba *as a liquid extract (acc. to Erg. B.6)* for the treatment of haemorrhages/bleeding has been reported in handbooks at least since 1941 (Ergänzungsbuch zum DAB 6, 1941 as mentioned in Blumenthal 1998 and Wichtl 1994). This preparation is not included in the monograph because clear manufacturing method and posology are lacking.

3. Non-Clinical Data

3.1. Overview of available pharmacological data regarding the herbal substance(s), herbal preparation(s) and relevant constituents thereof

In vitro studies with Capsella (preparations)

Studies with an ethanolic Capsella extract shown:

- *Anti-inflammatory activity* versus carrageenan-induced and dextran-induced rat paw oedema (Barnes *et al.* 2007; Kuroda & Tagaki, 1969).

- A reduction in capillary permeability in the guinea-pig induced by histamine and serotonin (Barnes *et al.* 2007; Kuroda & Tagaki, 1969).
- A purified substance from the alcohol extract exerted *contractile activity on rat uterus* equivalent to that of oxytocin (0.1 i.u.), which was unaffected by atropine but inhibited by competitive inhibitors of oxytocin (substance had some characteristics of a polypeptide) (Kuroda & Tagaki, 1968).

Studies on the isolated heart have reported *negative chronotropic and inotropic actions* in the guinea-pig and rabbit and *coronary vasodilatation* (Barnes *et al.* 2007; Jurisson, 1971).

Weak *antibacterial activity* mainly towards Gram-positive organisms has been reported (Barnes *et al.* 2007; Moskalenko, 1986).

The extract of dried or fresh plant material causes strong *contraction of the uterus and small intestines* of guinea-pigs, unaffected by atropine and diphenhydramine, but inhibited by papaverine (Barnes *et al.* 2007; Kuroda & Tagaki 1968; Jurisson, 1971; Khare, 2007).

Antioxidant activity of a methanolic extract from *Capsella* aerial parts was demonstrated *in vitro*, which might be due the high total phenolic content (Heo *et al.*, 2007).

***In vitro* studies with isolated components of Capsella**

Two unidentified alkaloid components of *Capsella* have been stated to elicit a physiological *activity on the uterus* (Barnes *et al.* 2007; Kuroda & Kaku 1969).

Flavonoid components isolated from *Capsella* have been reported to *reduce blood vessel permeability* in mice (Barnes *et al.* 2007; Jurisson, 1973).

Antineoplastic activity in rats has been reported for fumaric acid, which prevented the development of hepatic neoplasms when co-administered with the carcinogen 3-MeDAB (Barnes *et al.* 2007; Kuroda, 1977).

***In vivo* studies**

After oral or intraperitoneal administration of *Capsella* in mice, *diuresis* has been reported; the mode of action was stated to involve an increase in the glomerular filtration rate (Barnes *et al.* 2007; Kuroda & Tagaki, 1969).

A transient *decrease of blood pressure* was observed after intravenous administration of an ethanolic extract of *Capsella* to various kinds of animals (dogs, cats, rabbits, rats); the decreasing activity was antagonised by a β -adrenoreceptor blocker but not by atropine. The authors concluded that this action could not be attributable to other than cholinergic compounds (Kuroda & Kaku, 1969).

Following intra-arterial administration of *Capsella* extract, *increased coronary blood flow* has been reported in dogs and a slight *inhibitory effect on ouabain-induced ventricular fibrillation* in the rat together with a *chronotropic effect* after intraperitoneal injection (Barnes *et al.* 2007; Jurisson, 1971).

Capsella induced tracheal contractions in the guinea-pig were unaffected by adrenaline, which did inhibit acetylcholine induced contractions (Barnes *et al.* 2007; Jurisson, 1971).

A *CNS-depressant action* in mice has been demonstrated (potentiation of barbiturate-induced sleeping time) (Barnes *et al.* 2007; Jurisson, 1971).

After parenteral application muscarine-like effects have been reported with dose-dependant *lowering and elevation of blood pressure, positive inotropic and chronotropic cardiac effect, and increased uterine contraction* (Blumenthal, 1998).

Intraperitoneal injections of an ethanolic extract of *Capsella* (0.14 g/kg/day) exhibited an *inhibitory effect on Ehrlich solid tumour* in mice; treatment with the isolated compound fumaric acid showed this same activity (Kuroda *et al.*, 1976).

From the results of *in vitro* and animal studies, it was concluded that the active substance(s) responsible for the observed actions by *Capsella* on smooth muscle were neither acetylcholine nor histamine (Barnes *et al.* 2007; Kuroda & Tagaki 1968; Jurisson, 1971).

Assessor's comment:

Most of the cited articles contain very little data on study details; supportive studies on haemostatic activity are lacking.

3.2. Overview of available pharmacokinetic data regarding the herbal substance(s), herbal preparation(s) and relevant constituents thereof

No data with regard to absorption, distribution, metabolism, elimination, pharmacokinetic interactions with other medicinal products are available.

3.3. Overview of available toxicological data regarding the herbal substance(s)/herbal preparation(s) and constituents thereof

Acute toxicity

Capsella extracts have been reported to exhibit low toxicity in mice. Signs of toxicity were described as sedation, enlargement of pupils, paralysis of hind limbs, difficulty in respiration, and death by respiratory paralysis. LD₅₀ values reported are 1.5 g/kg body weight (mice, intraperitoneal injection) and 31.5 g/kg bodyweight (mice, subcutaneous injection) (Barnes *et al.* 2007; Jurisson, 1971).

Sinigrin

Following hydrolysis catalysed by the plant enzyme, myrosinase, the constituent sinigrin yields allyl isothiocyanate, a powerful irritant agent producing blisters on the skin. Isothiocyanates have been implicated in endemic goitre (hypothyroidism with thyroid enlargement) and have been reported to produce goitre in experimental animals (Barnes *et al.* 2007; Leung, 1980).

Assessor's comment:

No data on glucosinolate content or more specifically sinigrin content have been found. Not only total glucosinolate levels, but also glucosinolate composition may differ considerably between species, plants and even different tissues within the same plant (Hopkins, 2009). Sabri *et al.* (1975) report that the flowers of *Capsella* contain most sinigrin.

The metabolism of sinigrin in the human body is probably more complex. In a dynamic *in vitro* large-intestinal model, the production of allyl isothiocyanate from sinigrin was investigated after inoculation with a complex microflora of human origin. As only a small part (mean 19%) of sinigrin was converted into allyl isothiocyanate, it was suggested that allyl isothiocyanate is converted further into other, yet unknown, metabolites (Krul *et al.*, 2002).

Isothiocyanate can be further degraded to produce the thiocyanate ion. This component is able to cause goitre in humans when dietary iodine is insufficient. However there is no evidence to support a causative role for dietary glucosinolates in human goitre (New Zealand Food Safety Authority NZFSA, 2010).

The International Agency for Research on Cancer (IARC) reports that there is inadequate evidence in humans for the carcinogenicity of allyl isothiocyanate and limited evidence in experimental animals for the carcinogenicity of allyl isothiocyanate (IARC, 1999).

Safety of glucosinolates in the human diet has not been assessed by any national or international organisation as reported by the NZFSA (2010).

In relation to the above mentioned, the presence of glucosinolates in Capsella preparations which are administered in small quantities for a limited duration of time is considered not to be a concern for safety.

No data with regard to repeat-dose toxicity, genotoxicity, carcinogenicity, reproductive and developmental toxicity, local tolerance or other special studies are available.

3.4. Overall conclusions on non-clinical data

Studies on haemostatic activity have not been found. *In vitro* and *in vivo* studies with Capsella preparations or ingredients demonstrate potential anti-inflammatory, antioxidant, antibacterial activity, reduction of blood vessel permeability and stimulating activity on diverse smooth tissues.

There are limited toxicological non-clinical data.

Capsella extracts showed low toxicity in mice (IP injection LD₅₀: 1.5 g/kg, subcutaneous injection LD₅₀: 31.5 g/kg).

4. Clinical Data

No clinical data available.

4.1. Clinical Pharmacology

4.1.1. Overview of pharmacodynamic data regarding the herbal substance(s)/preparation(s) including data on relevant constituents

No clinical data available.

4.1.2. Overview of pharmacokinetic data regarding the herbal substance(s)/preparation(s) including data on relevant constituents

No clinical data available.

4.2. Clinical Efficacy

No clinical data available.

4.2.1. Dose response studies

No clinical data available.

4.2.2. Clinical studies (case studies and clinical trials)

No clinical data available.

4.2.3. Clinical studies in special populations (e.g. elderly and children)

No clinical data available.

4.3. Overall conclusions on clinical pharmacology and efficacy

The plausibility of efficacy for the specific indications of *Capsella bursa-pastoris* herb in the context of reduction of bleeding cannot be further substantiated by clinical data, as they are not available.

5. Clinical Safety/Pharmacovigilance

5.1. Overview of toxicological/safety data from clinical trials in humans

No clinical data available.

5.2. Patient exposure

No experimental data in humans is available.

From marketing experience data received from the Member States no pharmacovigilance actions have been undertaken and none have been reported following the use of Capsella preparations (based on data received from 12 Member States, situation on 17 August 2010).

5.3. Adverse events and serious adverse events and deaths

No clinical data available.

5.4. Laboratory findings

No clinical data available.

5.5. Safety in special populations and situations

As no explicit data have been found on intrinsic/extrinsic factors, drug interactions, use in pregnancy and lactation, overdose, drug abuse, withdrawal and rebound, effects on ability to drive or operate machinery or impairment of mental ability, following has to be taken into consideration:

The use of Capsella cannot be recommended during pregnancy and lactation, as reproductive toxicity data are missing. No fertility data are available.

No safety data have been found on the use of Capsella preparations in children for the relevant medicinal uses.

The potential for Capsella preparations to interact with other medicines administered concomitantly/concurrently should be considered, especially those with similar or opposing effects (Barnes *et al.*, 2007).

There is limited evidence from non-clinical studies that Capsella herba and/or certain isolated constituents may have hypotensive, diuretic and cardiac activities and effects on thyroid function (Barnes *et al.*, 2007).

Assessor's comment:

As these effects have mostly been reported in animals after non-oral administration of isolated components of *Capsella* and mechanisms of action are still unknown, the relevance of these data to human use remains unclear.

The Botanical Safety Handbook mentions the emmenagogue and uterine stimulating activity of *Capsella*, that large doses of extract may cause heart palpitations and that people with a history of kidney stones should be cautious (McGuffin *et al.*, 1997).

Assessor's comment: Causality of above mentioned effects with the use of *Capsella* is not clear, severity and frequency are unknown, as references are untraceable/missing. In other handbooks, these safety issues have not been mentioned.

5.6. Overall conclusions on clinical safety

Clinical safety data are very limited. However no safety problems concerning the traditional use of *Capsella bursa-pastoris* have been reported.

The use of *Capsella* should be avoided during pregnancy and lactation, as safety during pregnancy and lactation has not been established.

The oral use in adolescents under 18 years is not recommended because of concerns requiring medical advice.

6. Overall conclusions

Level of evidence

As clinical studies are missing, *Capsella* herba preparations cannot be considered for well-established use indications; only Traditional Use (TU) is applicable. Results of well designed randomised clinical studies will be needed to verify the clinical relevance of the described pharmacological effects.

The establishment of a Community list entry is not possible, because studies on genotoxicity, mutagenic and carcinogenic properties are lacking.

Safety

No published reports on serious side effects after use of *Capsella* containing preparations have been found and no pharmacovigilance issues been reported by Member States marketing *Capsella* products. See also 5.2 Patient exposure.

No experimental data is available on possible toxicity of *Capsella bursa-pastoris* and preparations thereof. However, in view of the results of the non-clinical studies and the long period of marketing experience without reports of adverse reactions, the specified *Capsella bursa-pastoris* herbal preparations can be considered as proven not to be harmful in the specified conditions of use as required by Article 16a 1 (e) of Directive 2004/24/EC.

Some special warnings are stated in the Botanical Safety Handbook:

- Individuals with a history of kidney stones should be cautious
- Large doses of extract may cause heart palpitations (Mc Guffin *et al.*, 1997).

However, as justifying data on clinical relevance are lacking and as these warnings are not mentioned in other handbooks, it is expected that the recommended use is safe. Therefore, these warnings are not included in the monograph.

Indication

The long-standing use and experience in bleeding and other health problems support the safe use of the specified herbal preparations in the context of reduction of bleeding:

“Traditional herbal medicinal product for the reduction of heavy menstrual bleeding in women with regular menstrual cycles, after serious conditions have been excluded by a medical doctor.”

The efficacy is only plausible on basis of long-standing use and experience, as required by Article 16a 1 (e) of Directive 2004/24/EC and is not supported by pharmacological data.

Posology

For the proposed indication, use in children is not relevant.

Adults	Adolescents
<p>Oral use</p> <p>Comminuted herbal substance as herba tea: 1-5 g as a single dose, 2-4 times daily (daily dose: 3-20 g)</p> <p>Liquid extract: (DER 1:1), extraction solvent ethanol 25% V/V: 1-4 ml as a single dose, 3 times daily (daily dose: 3-12 ml)</p>	<p>Oral use</p> <p>The oral use in adolescents under 18 years of age is not recommended because of concerns requiring medical advice.</p>

Duration of use

Oral use

If the symptoms persist during the use of the medicinal product, a doctor or a qualified health care practitioner should be consulted.

Monograph

The monograph for *Capsella herba* covers the comminuted herbal substance and liquid extract above mentioned only for oral use (other preparations may be added later in the monograph, when clear specifications, study data and/or new market information will be made available).

Annex

List of references