EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Committee on Herbal Medicinal Products (HMPC)

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

Based on Article 10a of Directive 2001/83/EC as amended (well-established use)

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

Draft

Herbal substance(s) (binomial scientific name of the plant, including plant part)	*Capsella bursa-pastoris* (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.
Rapporteur	
Assessor(s)	

Note: This Assessment Report is published to support the release for public consultation of the draft Community herbal monograph on *Capsella bursa-pastoris* (L.) Medikus, herba. It should be noted that this document is a working document, not yet fully edited, and which shall be further developed after the release for consultation of the monograph. Interested parties are welcome to submit comments to the HMPC secretariat, which the Rapporteur and the MLWP will take into consideration but no 'overview of comments received during the public consultation' will be prepared in relation to the comments that will be received on this assessment report. The publication of this draft assessment report has been agreed to facilitate the understanding by Interested Parties of the assessment that has been carried out so far and led to the preparation of the draft monograph.

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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).

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

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, tricin, 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-methylsulfinylnoyl and 10-methylsulfinyldecyl glucosinulates (in seeds), carotenoids, ascorbic acid, vitamin K, cardenolide, calcium and potassium salts, unidentified alkaloids, mustardoil 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 II.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 ω6-PUFAS was found in Capsella. The amount of erudic acid (C22:1ω9), 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 low % of Na content (Guil-Guerrero et al., 1999).

Analysis of herbs and their decoctums and tinctures by ICP-OES 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).

However results of analysis should cautiously be interpreted: 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 next paragraph.

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	Dosaging	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:

Austria: Menodoron;

France: Hemoluol[1], Histo-Fluine P, Tisane Provencale no 3, Tisanes de lÁbbe 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 (not mandatory field)**
Austria	☐ MA	☐ TRAD	☐ Other TRAD	☐ Other Specify:	No medicinal products on market with Capsella
Belgium	☐ MA	☐ TRAD	☐ Other TRAD	☐ Other Specify:	
Bulgaria	☐ MA	☐ TRAD	☐ Other TRAD	☐ Other Specify:	No products with MA; no info on food supplements
Cyprus	☐ MA	☐ TRAD	☐ Other TRAD	☐ Other Specify:	
Czech Republic	☐ MA	☐ TRAD	☐ Other TRAD	☐ Other Specify:	
Denmark	☐ MA	☐ TRAD	☐ Other TRAD	☐ Other Specify:	No medicinal products on market with Capsella
Estonia	☐ MA	☐ TRAD	☐ Other TRAD	☐ Other Specify:	No medicinal products on market with Capsella
Finland	☐ MA	☐ TRAD	☐ Other TRAD	☐ Other Specify:	
France	☐ MA	☐ TRAD	☐ Other TRAD	☐ Other Specify:	Only in combination products (2 WEU-products containing herbals + chemical component; 1 TU - product containing only herbals)
Germany	☒ MA	☐ TRAD	☐ Other TRAD	☐ Other Specify:	WEU: 2 herbal teas with Capsella as single ingredient TU: 1 combination product for tea preparation
Greece	☐ MA	☐ TRAD	☐ Other TRAD	☐ Other Specify:	
Hungary	☐ MA	☐ TRAD	☐ Other TRAD	☐ Other Specify:	1 combination product for tea preparation as THMP, 1 herbal tea with Capsella as single ingredient on market as food

[1] This preparation is discontinued or no longer marketed

Member State	Regulatory Status				Comments (not mandatory field)
Iceland	☐ MA	☐ TRAD	☐ Other TRAD	☐ Other Specify:	
Ireland	☐ MA	☐ TRAD	☐ Other TRAD	☐ Other Specify:	
Italy	☐ MA	☐ TRAD	☐ Other TRAD	☐ Other Specify:	
Latvia	☐ MA	☐ TRAD	☐ Other TRAD	☐ Other Specify:	No medicinal products on market with Capsella
Liechtenstein	☐ MA	☐ TRAD	☐ Other TRAD	☐ Other Specify:	
Lithuania	☐ MA	☐ TRAD	☐ Other TRAD	☐ Other Specify:	
Luxemburg	☐ MA	☐ TRAD	☐ Other TRAD	☐ Other Specify:	
Malta	☐ MA	☐ TRAD	☐ Other TRAD	☐ Other Specify:	
The Netherlands	☐ MA	☐ TRAD	☐ Other TRAD	☐ Other Specify:	No medicinal products on market with Capsella
Norway	☐ MA	☐ TRAD	☐ Other TRAD	☐ Other Specify:	
Poland	☐ MA	☐ TRAD	☐ Other TRAD	☐ Other Specify:	
Portugal	☐ MA	☐ TRAD	☐ Other TRAD	☐ Other Specify:	
Romania	☐ MA	☐ TRAD	☐ Other TRAD	☐ Other Specify:	
Slovak Republic	☐ MA	☐ TRAD	☐ Other TRAD	☐ Other Specify:	No medicinal products on market with Capsella
Slovenia	☐ MA	☐ TRAD	☐ Other TRAD	☐ Other Specify:	
Spain	☐ MA	☒ TRAD	☐ Other TRAD	☐ Other Specify:	Only in combination products
Sweden	☐ MA	☐ TRAD	☐ Other TRAD	☐ Other Specify:	
United Kingdom	☐ MA	☒ TRAD	☐ Other TRAD	☐ 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

Databases assessed (date, search terms) and other sources used.

If applicable (data availability), inclusion and exclusion criteria for literature, ideally differentiated between the main topics Non-clinical, Clinical, Safety.

Cross-reference to the list of references in Annex, which should list separately the references supporting the assessment report and the references used but which do not support the assessment report.

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 problem s (diarrhea 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 addressed 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 hemorrhaging, and its continuous use in folk medicine to treat dysmenorrhea. 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 haemorhaging is obsolete). It is used in European traditional medicine for preventing or arresting hemorrhage, more specifically to treat dysmenorrhea.

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 hemorrhages 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 hemostatic agent for treatment of chyluria (fat globules in the urine) and hematuria (Herbalgram, 2008).

For each herbal preparation, provide evidence of history and extent of use preferably classified whether predominantly European or non-European tradition, and the more recent/current use.

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

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

Blood/Hemorrhages/Bleeding

reference	indication	preparation
Felter, 1922	Passive hemorrhages (and slight stimulant in amenorrhoea)	- Specific Medicine Capsella Infusum Capsella
Steinmetz, 1954	Hemostatic agent for all kind of bleedings	- Infusion - Extractum *Capsella Bursae pastoris* 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	Hemostatic agent (menstrual and nose bleedings)	- Infusion - Thlaspi bursae-pastoris ø (1:2 fresh whole plant in 50 % alcohol v/v)
Wichtl, 1994	As hemostatic agent	- Infusion - Dry extract (DER 4.1:1; solvent water)
Barnes et al., 2007	Anti-hemorrhagic (traditionally used for hematemesis, 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 hemorrhage, 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.(ø) - Extractum fluidum bursae pastoris
Wichtl, 1994	Dysmenorrhea	- Infusion - Dry extract (DER 4.1:1; solvent water)
Mc Guffin, 1997	As emmenagogue/uterine stimulant	
Blumenthal, 1998; Schulz et al., 1998	Symptomatic treatment of mild menorrhagia and metrorrhagia	- Infusion - Fluidextract (acc. to Erg. B. 6)
Barnes et al., 2007	menorrhagia	- Infusion - Liquid extract (1:1 in 25% alcohol)
Khare, 2007	menorrhagia	- Juice extracts

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 et al., 2007	Urinary antiseptic, diarrhoea and acute catarrhal cystitis	- Infusion - Liquid extract (1:1 in 25% alcohol)
Khare, 2007	Haemorrhages from renal and genitourinary 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 symptomatical 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 diarrhea 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 et al., 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, dysmenorrhea
Blumenthal, 1998		10-15 g equivalent preparations	Symptomatic treatment of mild menorrhagia and metrorrhagia
Schulz et al., 1998		5-15 g	Symptomatic treatment of mild menorrhagia and metrorrhagia

Herbal substance and comminuted herbal substance for tea preparation *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 ¾ of water	dose freely	As haemostatic agent; nosebleeds and superficial bleeding skin injuries

Herbal preparation: Liquid extract 1:1 in 25% alcohol

reference	single dose	daily dose	indication
BHP, 1983; Barnes et al., 2007	1-4 ml	3-12 ml	Menorrhagia, haematemesis, haematuria, diarrhea 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, dysmenorrhea

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' (Bühring 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:

The use of Capsella in children is described in only one reference, the duration of experience with medicinal use in children is unknown. Furthermore (pre-) clinical data to support the safe use in children is lacking. Therefore the use in children is not included in the monograph.

Other preparations

In the consulted documentation 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 bursinicum			Bombelon, 1888 (in Kuroda 1969)
Specific Medicine Capsella	1-60 drops		Felter, 1922
Infusion (of fresh herb, 3j to water 0j)		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 bursae-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 et al., 2007; Khare, 2007

Conlusion

Oral administration and topical application are the routes of administration for Capsella herba preparations in the recommended traditional indications. From the information in the handbooks the following posology data for the specified preparations can be concluded.

Proposed posology for adults (tea for 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.

The remark should be added that 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 and lack data on posology. For acceptance in the monograph, the traditional use of the individual preparations based on Capsella should be evaluated:

- The use Capsella herba *as an infusion* for the treatment of haemorrhages has been reported at least since 1922 and can be accepted according to the 30 years of use in medicinal practice 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 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 30 years of use in medicinal practice 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, 1941 as mentioned in Blumenthal 1998 and Wichtl 1994). This preparation is not included in the monograph because a 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 exhibited

- *Anti-inflammatory activity* versus carrageenan-induced and dextran-induced rat paw oedema (Barnes et al.; Kuroda & Tagaki, 1969).
- A *reduction in capillary permeability* in the guinea-pig induced by histamine and serotonin (Barnes et al.; 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.; Jurisson, 1971).

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

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

Antioxidant activity of a methanolic extract form 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.; Kuroda & Kaku 1969).

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

Antineoplastic acitvity 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.; 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.; Kuroda & Tagaki, 1969).

A transient *decrease of bloodpressure* 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.; Jurisson, 1971).

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

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

After parenteral application muscarine-like effects have been reported with dose-dependant *lowering and elevation of bloodpressur*e, *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 tumor* 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.; 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.; Jurisson, 1971).

Sinigrin

Following hydrolysis catalysed by the plant enzyme, myrosinase, the constituent sinigrin yields allylisothiocyanate, a powerfull 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.; G41- 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 (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 glucosinulates in Capsella preparations which are administered in small quantities for a limited duration of time is considered not to be a concern of 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 preclinical 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 safety data have been found on the use of Capsella preparations in children.

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 preclinical 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, 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 children under 18 years is not recommended.

6. Overall conclusions

Classification

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.

A list entry is not applicable, 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 (preparations of) *Capsella bursa-pastoris*. However, in view of the results of the preclinical 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 Art. 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 cautiously
- Large doses of extract may cause heart palpitations (Mc Guffin, 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 will not be included in the monograph.

Use

The long traditional experience in bleeding and many other health problems, support the safe use of the specified herbal preparations in the context of reduction of bleeding.

Capsella herba is used for the reduction of heavy menstrual bleeding in women with regular menstrual cycles.

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

Posology

Adults and elderly	**Children and adolescents**
Oral use Comminuted herbal substance as tea: 1-5 g as a single dose, 2-4 times daily (daily dosage: 3-20 g) Liquid extract: (DER 1:1), extraction solvent ethanol 25% V/V: 1-4 ml 3 times daily	**Oral use** The oral use in children and adolescents under 18 years of age is not recommended (see section 4.4 'Special warnings and precautions for use').

Duration of use

Oral use

If heavy menstrual bleeding is not reduced after 3 cycles, a doctor should be consulted.

Monograph

The monograph for Capsella herba will be based on the Capsella herbal substance to be used in above mentioned liquid dosage forms only for oral use. (other preparations may be added, when clear specifications, study data and/or more market information will be made available).

Annex

List of references