EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

12 November 2013
EMA/HMPC/317317/2012
Committee on Herbal Medicinal Products (HMPC)

Assessment report on *Phaseolus vulgaris* L., fructus sine semine

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)	*Phaseolus vulgaris* L., fructus sine semine
Herbal preparation(s)	Comminuted herbal substance
Pharmaceutical form(s)	Comminuted herbal substance as herbal tea 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)

Phaseolus vulgaris L. belongs to the family of *Fabaceae*.
The herbal substance consists of the dried pericarpium freed of the seeds of *Phaseolus vulgaris* L. According to the DAC 1986, the water soluble extractive is not less than 12%; the seed fragments are not more than 4%, and foreign matter not more than 2%. Ash is not more than 8% (DAC 1986).

In English, it is referred to as green bean, kidney bean, French bean, common bean or haricot bean. It is referred to as *Fructus phaseoli sine semine* or *Phaseoli pericarpium* in Latin, Bohnenhülsen and Schminckbohne in German and 'Gousses d'haricot' in French.

Phaseolus is known as an ancient cultivated plant. The herbal substance comes from cultivated plants grown in various European countries (amongst others Bulgaria, Hungary, the former USSR and former Yugoslavia) (Wichtl 1984; Wichtl 1994; Czech Pharmaceutical Codex 1993).

The herbal substance is described in other compendia and textbooks.
Kidney bean pods consist of the fruit wall, freed from the seeds. The material is in the form of yellowish white, somewhat curled, thin pieces of the up to 15 cm long fruit wall. The outside surface is pale yellow and slightly wrinkled; the inside is covered with a whitish, shiny membrane (endocarp and inner mesocarp layers). Occasionally, yellow fragments of the stalks are present.
The herbal substance is without smell and with slightly mucilaginous taste. Authentication of the plant is done macro- and microscopically. The exocarp has a strong wrinkled cuticle, roundish stomata, and cicatrices. In the outer layers, the mesocarp consists of short, spindle-shaped, thickened cells. In the inner layers of the mesocarp crystals are present with a conspicuous feature. Adulteration of the herbal substance is seldom encountered (Wichtl 1994; Czech Pharmaceutical Codex 1993).

The Czech Pharmaceutical Codex (1993) describes identification tests:

a) Legume freed from seeds. Often slightly screw-like curled, up to 15 cm long and up to 2 cm wide, on both sides shortly beak-like pointed, on the lower end often with the rest of stalk. The outside surface is yellowish matt, inside shiny white with easily peelable membrane.

b) Microscopy. Epidermis of the exocarp consists of polygonal, equilateral cells with scars after trichomes and circular stomata without adjacent cells, with firmly wrinkled cuticle. The mesocarp consists of several layers of thick-walled, slightly longitudinally oblong, fusiform, firmly incrassate, fibrous cells, several layers of parenchyma, sometimes with small crystals of calcium oxalate and with numerous anastomic vascular bundles. Bigger vascular bundles over phloem with vagina from roughly dotted fibres with wide lumen. Epidermis of the endocarp consists of thick-walled, yellow, longitudinally oblong cells with isolated rather cavernous stomata, easily detachable from the pericarp.

According to the Czech Pharmaceutical Codex (1993), the following characteristics should be respected:

a) Foreign matters (ČSL 4, page 100/I)
b) Different coloured drug maximum 5%
c) Foreign organic matter maximum 1%
d) Inorganic matter maximum 0.5%
e) Loss on drying maximum 10% (ČSL 4, page 100/I)

f) Ash maximum 7% (ČSL 4, page 100/I)
g) Asch insoluble in hydrochloric acid maximum 2% (ČSL 4, page 100/I)
The herbal substance contains arginine and silicic acid, as well as chromium salts (cf. antidiabetic activity).

Assessor's comment
The composition of the pods is different from that of the beans. The kidney beans themselves *(Phaseolus vulgaris fructus)* contain several phytochemicals, whereof the most important compounds are described as follows:
The carbohydrates which can be divided in starch and non-starch polysaccharides, which include resistant starch, soluble and insoluble dietary fibre, and non-digestible oligosaccharides.
Polyphenols, such as flavonoids, appear to have an antioxidant activity and determine the seed colour of the beans.
A specific derivate of isoflavonoids, found in *Phaseolus vulgaris*, is phaseolin, an alpha-amylase inhibitor.
The lectins, including phytohaemagglutinin (PHA), show a haemagglutinin activity. These compounds are heat sensitive, which makes it possible to reduce the lectin activity by extrusion or home cooking. Trypsin inhibitors are also influenced by extrusion and home cooking, because these methods reduce the protease inhibiting activity (Reynoso-Camacho *et al.* 2006; Ocho-Anin *et al.* 2010).

It should be noted that the beans themselves are not considered in the monograph and that their use is different from that of the pods. Only preparations that are exposed to heat during manufacturing are recommended for human use. Since lectins and trypsin inhibitors are heat sensitive, their activity is reduced and, with that, the toxicity of *Phaseolus vulgaris* (see also section 3.3). The extracts contain a high amount of alpha-amylase inhibitor, whose activity on weight control has been clinically investigated. Therapeutic use of seed preparations cannot be considered as belonging to the tradition which is described in the present assessment report on the pods.

- Herbal preparation(s)

The comminuted herbal substance is used as a herbal tea for oral use.

- Combinations of herbal substance(s) and/or herbal preparation(s) including a description of vitamin(s) and/or mineral(s) as ingredients of traditional combination herbal medicinal products assessed, where applicable.

Not applicable.

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

Regulatory status overview

Member State	Regulatory Status				Comments
Austria	☐ MA	☐ TRAD	☐ Other TRAD	☐ Other Specify:	No registered products
Belgium	☐ MA	☐ TRAD	☐ Other TRAD	☐ Other Specify:	No registered products
Bulgaria	☐ MA	☐ TRAD	☐ Other TRAD	☐ Other Specify:	No registered products
Cyprus	☐ MA	☐ TRAD	☐ Other TRAD	☐ Other Specify:	
Croatia	☐ MA	☐ TRAD	☐ Other TRAD	☐ Other Specify:	
Czech Republic	☐ MA	☐ TRAD	☐ Other TRAD	☒ Other Specify:	Only in combined preparations
Denmark	☐ MA	☐ TRAD	☐ Other TRAD	☐ Other Specify:	No registered products
Estonia	☐ MA	☐ TRAD	☐ Other TRAD	☐ Other Specify:	No registered products
Finland	☐ MA	☐ TRAD	☐ Other TRAD	☐ Other Specify:	No registered products
France	☐ MA	☐ TRAD	☐ Other TRAD	☐ Other Specify:	No registered products
Germany	☐ MA	☐ TRAD	☐ Other TRAD	☒ Other Specify:	One registered combination product
Greece	☐ MA	☐ TRAD	☐ Other TRAD	☐ Other Specify:	No registered products
Hungary	☐ MA	☐ TRAD	☐ Other TRAD	☒ Other Specify:	Only in combined preparations
Iceland	☐ MA	☐ TRAD	☐ Other TRAD	☐ Other Specify:	
Ireland	☐ MA	☐ TRAD	☐ Other TRAD	☐ Other Specify:	
Italy	☐ MA	☐ TRAD	☐ Other TRAD	☐ Other Specify:	No registered products
Latvia	☐ MA	☐ TRAD	☐ Other TRAD	☐ Other Specify:	
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 registered products
Norway	☐ MA	☐ TRAD	☐ Other TRAD	☐ Other Specify:	
Poland	☐ MA	☐ TRAD	☐ Other TRAD	☐ Other Specify:	
Portugal	☐ MA	☐ TRAD	☐ Other TRAD	☐ Other Specify:	No registered products
Romania	☐ MA	☐ TRAD	☐ Other TRAD	☒ Other Specify:	Only combined products
Slovak Republic	☐ MA	☐ TRAD	☐ Other TRAD	☐ Other Specify:	
Slovenia	☐ MA	☐ TRAD	☐ Other TRAD	☐ Other Specify:	
Spain	☐ MA	☐ TRAD	☐ Other TRAD	☐ Other Specify:	No registered products
Sweden	☐ MA	☐ TRAD	☐ Other TRAD	☐ Other Specify:	No registered products
United Kingdom	☐ MA	☐ TRAD	☐ Other TRAD	☐ Other Specify:	No registered products

MA: Marketing Authorisation

TRAD: Traditional Use Registration

Other TRAD: Other national Traditional systems of registration

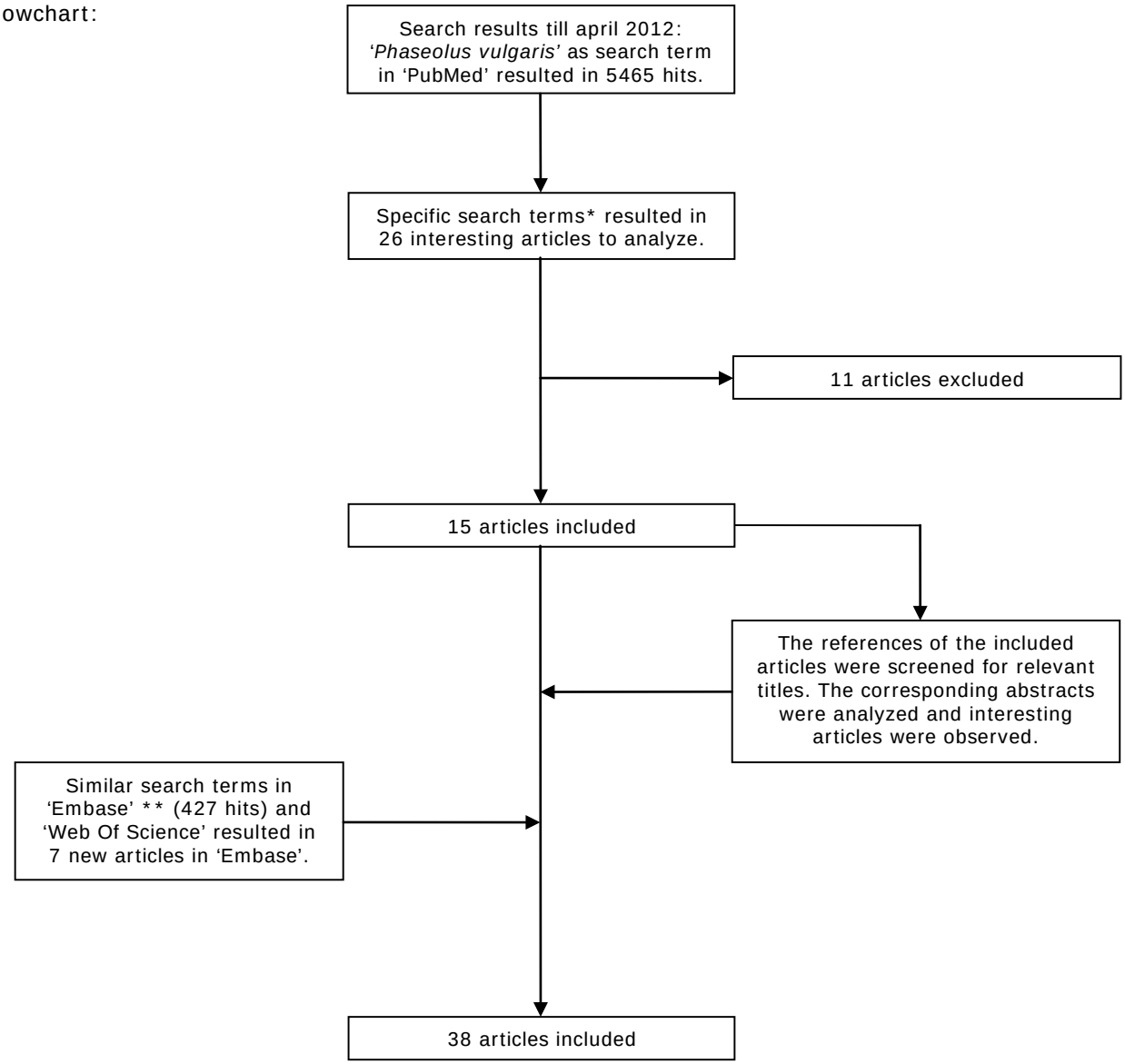
Other: If known, it should be specified or otherwise add 'Not Known'

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

Publications from PubMed were used after limiting the search by including only articles where *Phaseolus vulgaris* was mentioned in title and/or abstract. The promising references of the found publications were also investigated either in PubMed, local journals or specific websites. Other sources were a number of handbooks available to the Rapporteur (see list of references).

Flowchart:



* Specific search terms in PubMed:

- "*Phaseolus*/adverse effects"[Mesh] OR "*Phaseolus*/poisoning"[Mesh] OR "*Phaseolus*/toxicity"[Mesh]
- (*phaseolus*[Title/Abstract] AND vulgaris[Title/Abstract]) AND (Clinical Trial[ptyp] OR Randomised Controlled Trial[ptyp] OR Review[ptyp])
- (*phaseolus*[Title/Abstract] AND vulgaris[Title/Abstract]) AND *in vitro*[ptyp]

- *phaseolus*[Title/Abstract] AND vulgaris[Title/Abstract] AND weight[Title/Abstract] AND loss[Title/Abstract]
- *phaseolus*[Title/Abstract] AND vulgaris[Title/Abstract] AND diabetes[Title/Abstract]

** Specific search terms in Embase:

- "*Phaseolus vulgaris* extract"
- *'Phaseolus'*/syn AND *vulgaris* AND [human]/lim AND [english]lim AND [abstracts]/lim

Further narrowing of the number of articles used in support of the AR took place during the establishment of the monograph.

2. Historical data on medicinal use

2.1. Information on period of medicinal use in the Community

Historical research (Helmstädter 2010)

Bean pods were already described by Dodoens (1608) as having a diuretic activity and compared to Asparagus for this action. *Phaseolus vulgaris* preparations were described in medical records in 1908. M. Kaufmann (Germany) wrote a review of oral drugs with supposed antidiabetic activity. He mentioned three case studies where bean pod tea was tested, but appeared to be ineffective. A published article in 1923 by J. Bertram Collip (Canada) described the application of an alcoholic extract of 'bean greens' (leaves and stems) to rabbits. After 12 hours, a reduction by 20% of blood sugar levels was obtained after an initial rise. In 1927, Prof. E. Kaufmann (Germany) published a series of articles where aqueous and ethanolic extracts of bean pods were part of the experiments. There was a moderate hypoglycaemic effect in normal rabbits. Furthermore, patients of a clinical study showed decreases of blood sugar values within 4 hours. Geβner and Siebert (Germany) investigated in 1928 the effect of aqueous and alcoholic extracts of bean pods in rabbits. The results showed decreases in blood glucose values. Also in 1928, Eisler and Portheim (Austria) performed *in vitro* studies with alcoholic extracts of bean pods. The next investigators were Gohr and Hilgenberg (Germany) in 1929. They used the same commercial extract as that studied by Geβner and Siebert, but administered it to dogs. Only in hyperglycaemic dogs, significant decreases were obtained. The same extract was used by Gebhardt (Germany) in 1930, who investigated the effect in starving rabbits and diabetic patients. Since not all rabbits/patients showed reductions of the blood sugar values, he considered the extract as not effective. In 1932, Hartleb (Poland) obtained contradictory results after administration of an extract in healthy and diabetic patients. He concluded that the extract's effect was unpredictable, but may have some use in the treatment of diabetes. Lapp (Austria) claimed in 1937 that bean pod tea reduced the blood glucose levels of healthy people, but not in diabetic patients.

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

Table 1: Overview of traditional uses of bean pods

Traditional indications	**Source**
Bean pod tea (without seeds)/tablet: - Mildly diuretic Tablets/combination therapy: - Adjuvant with diabetes mellitus	Braun (1981)

Bean pod tea: - Diuretic - Weak anti-diabetic	Wichtl (1984), Wichtl (1994)
Bean pod tea (without seeds)/powder/mother tincture: - Mildly diuretic - Adjuvant with arthritis; gout; diabetes mellitus; obesity	Van Hellemont (1985)
Bean pod tea: - Diuretic	Reuter (1997)
Bean pod tea (without seeds)/mother tincture: - Weak antidiabetic - Diuretic	Delfosse (1998)
Bean pods or extract (oral): - Obesity; obtain constant weight level after losing weight. - Diabetes type II; insulin resistance; metabolic syndrome; reactive hypoglycaemia Bean pod (oral): - Adjuvant with arthrose; arthritis; gout; oedema; hypertension; kidney- and bladder disorders - Constipation	Verhelst (2010)

Since 2001 investigations were more concentrated on the beans themselves (Phaseoli vulgaris semen). However, commenting upon the results obtained with the beans is out of scope of this assessment report, as the use of bean extracts does not belong to the tradition of 30 years reported in the present document.

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

Austria

*Phaseolu*s (bean pods) is present in 2 herbal combination teas, which are only sold in that pharmacy where they are manufactured, therefore only a very restricted and only local importance can be given to Phaseolus containing products.

Bulgaria

There are no products containing *Phaseolus vulgaris* with marketing authorisation or registration in Bulgaria. There is no information available for food supplements.

Czech Republic

There is a herbal tea on the market since 1969 containing Phaseoli fructus sine semine as well as Myrtilli herba, Salviae officinalis herba, Galegae herba, Polygoni avicularis herba, Taraxaci radix cum herba, Rubi fruticosi folium, Foeniculi fructus and Bardanae radix.
Indication: traditionally used as an adjuvant in diabetes.

Phaseoli fructus sine semine has been described in the Český farmaceutický kodex (Czech Pharmaceutical Codex) since 1993, with the following recommended dosage: for oral use, single dose = 3 g in a form of a decoction; pharmacological group: phytopharmaceutical (diuretic, antidiabetic).

Estonia

There are no medicinal products containing *Phaseolus vulgaris* in Estonia. Other products containing this plant are probably classified as food supplements, under notification at the Veterinary and Food Board.

Germany

In Germany, there is one authorised combination product (tablets). It contains Phaseoli fructus sine semine and Urticae herba, Rosae pseudofructus cum fructibus, Equiseti herba, Betulae folium. Indication: Traditionally used to support the elimination function of the kidney.

Hungary

There are no mono-preparations with *Phaseolus* on the market. *Phaseolus vulgaris* (pericarpium and legumen) is in two tea-mixtures used to keep the diet in the case of predisposition for diabetes.

Romania

The NAMMD authorised in 2001 Phaseoli fructus sine seminibus as raw material (there was such a requirement before accession to the EU) which, further on, was included in a combination product, authorised in 2003 as adjuvant in diabetes mellitus. No products with Phaseoli fructus sine seminibus as single component have been authorised by NAMMD.

Table 2: Information about therapeutic regimen supporting traditional use

Posology: form / per dose / per day (bean pods)	**Source**
- Tea: 1 teaspoon bean pods (without seeds) per cup.	Braun (1981)
- Tea: Pour boiling water over 2.5 g bean pods (without seeds), wait 10 to 15 minutes before straining.	Wichtl (1984), Wichtl (1994)
- Bean pod tea: 2.5 g a cup, 8 to 12 hours in cold water, multiple cups daily.	Van Hellemont (1985)
- Tea: 5 to 15 g bean pods.	Reuter (1997)
- Tea: Pour boiling water over 2.5 g bean pods (without seeds), wait 10 to 15 minutes before straining.	Delfosse (1998)
- Bean pod tea (without seeds): 1) 2.5 g a cup, 8 to 12 hours in cold water, multiple cups daily. 2) Pour boiling water over 2.5 g, wait 10 to 15 minutes before straining.	Verhelst (2010)
- Phaseoli pericarpium: Tea: pour boiling water over 2.5 g, wait 10 to 15 minutes before drinking. Daily dose: 5 to 15 g	Hager's CDRom (2012)

Table 3: Other information about therapeutic regimen

Posology: form / per dose / per day (bean pods)	Source
- Tablets: 2 to 3 times a day 1 tablet (diuretic): no specification given. 3 times a day 3 to 4 tablets (antidiabetic): no specification given. - Combination therapy: *Phaseolus vulgaris* combined with *Syzygium* (Syamplex), 3 times a day 20 droplets of the preparation.	Braun (1981)
- Tea: Component of bladder and kidney tea (tea bags).	Wichtl (1984), (Wichtl 1994)
- Bean pods powder (without seeds): single dosage of 150 to 400 mg, daily dosage of 600 to 1,200 mg. - Mother tincture: 3 x 30 droplets daily.	Van Hellemont (1985)
- Mother tincture: 3 x 30 droplets daily.	Delfosse (1998)
Daily dosage is equivalent to 5-15 g bean pods. - Bean pods powder (without seeds): 3 x 200 to 400 mg daily, respectively before and during the meal. Indications include to avoid reactional hypoglycaemia. - Mother tincture: 3 x 30 droplets daily.	Verhelst (2010)

3. Non-Clinical Data

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

Bean pods

Research on hypoglycaemic effect (overview by Helmstädter 2010)

Roman-Ramos *et al.* (Mexico) discovered in 1991 hypoglycaemic effects of an aqueous extract after administration to rabbits. Similar results were observed in 1995 with decocted *Phaseolus vulgaris* pods.

In contrast to the two previous studies, no effect of an aqueous extract (prepared from 15 g of powdered pods in 300 ml of water), given in a dose of 25 g of extract/kg, was seen on streptozotocin diabetic mice in an oral glucose tolerance test by Neef *et al.* in 1995.

An article published in 2003 by Pari and Venkateswaran mentions the glucose lowering effects of a hot aqueous extract prepared from *Phaseolus vulgaris* pods (200 mg/kg) on streptozotocin diabetic rats. The administration of the extract resulted in a significant hypoglycaemic effect. Both the extract and glibenclamide reversed the decrease of the hexokinase and glucose-6-phosphate dehydrogenase in the liver and decreased the gluconeogenic enzymes. The effect of the extract appeared to exceed that of glibenclamide. In 2004, the authors confirmed the results in a similar, additional study by finding a decrease in blood sugar levels and an increase in insulin levels comparable to these of glibenclamide.

Table 4: Studies on hypoglycaemic effect

Reference	Experimental model	Intervention	Outcome
Roman-Ramos *et al.* (1995)	27 adult normoglycaemic New Zealand rabbits, weighing 2.5 to 3.5 kg. The rats were fed with Purina nutri-cubes and water. Decocted bean pods (4 ml/kg body weight)	Eight studies were performed on all rabbits: two with water (1st and 5th week), two with tolbutamide (2nd and 6th week) and four with plant preparations (3rd, 4th, 7th and 8th week; 8th week of group 3: *Phaseolus vulgaris* decoction). Before each study, all rats were submitted to a fasting of 16 h. All products were gastrically administrated, where after a 50% dextrose solution (4 ml/kg) was infused subcutaneously and repeated after 60 min.	Significant ($P<0.01$) decreases of the blood sugar values and the hyperglycaemic peak were obtained in comparison with the control values (water).
Pari *et al.* (2004)	50 male albino Wistar rats, weighing 170 to 200 g. The 20 normal and 30 streptozotocin diabetic surviving rats were equally divided in respectively 2 and 3 groups. Extract of dried pods of *Phaseolus vulgaris*.	Intra-gastrically daily for 45 days. Extract of dried pods of *Phaseolus vulgaris*: 200 mg/kg body weight	The fasting blood glucose was lower in all rats treated with the extract, but in the diabetic rats a significant difference was observed. The plasma insulin values were significantly higher in all treated rats.

Table extracted from Roman-Ramos et al. 1995: Significant (P<0.01) decrease of the blood sugar values.

Table 4
Glucose tolerance test in healthy rabbits with gastric administration of water, tolbutamide or plant preparations (group 3)

Study/preparation	Blood glucose mg/dl % (mean ± S.E.M.)					
	In fasting	60 min	120 min	180 min	240 min	300 min
Water (control) ($n = 18$)	77.8 ± 1.7	186.8 ± 8.7	234.9 ± 8.0	197.0 ± 7.4	158.9 ± 6.8	117.1 ± 5.5
Tolbutamide ($n = 18$)	81.1 ± 1.3	163.3 ± 6.3*	195.3 ± 5.2***	149.4 ± 4.7***	139.1 ± 5.3	95.0 ± 3.4*
Allium sativum ($n = 9$)	85.0 ± 2.6	177.4 ± 13.2	212.0 ± 15.6	189.0 ± 13.0	140.9 ± 6.3	112.8 ± 4.8
Brassica oleracea var. *botrytis* ($n = 9$)	78.6 ± 4.1	179.5 ± 11.2	204.2 ± 11.8*	182.8 ± 12.0	158.4 ± 3.3	130.4 ± 4.3
Lactuca sativa var. *romana* ($n = 9$)	76.5 ± 3.2	179.6 ± 13.8	229.1 ± 6.4	188.3 ± 11.3	153.1 ± 4.0	103.5 ± 5.6
Phaseolus vulgaris ($n = 9$)	79.2 ± 2.7	149.0 ± 8.0**	185.0 ± 8.2***	158.6 ± 6.8**	116.3 ± 3.8***	89.1 ± 3.4**

Significantly different from control: *$P < 0.05$; **$P < 0.01$; ***$P < 0.001$.

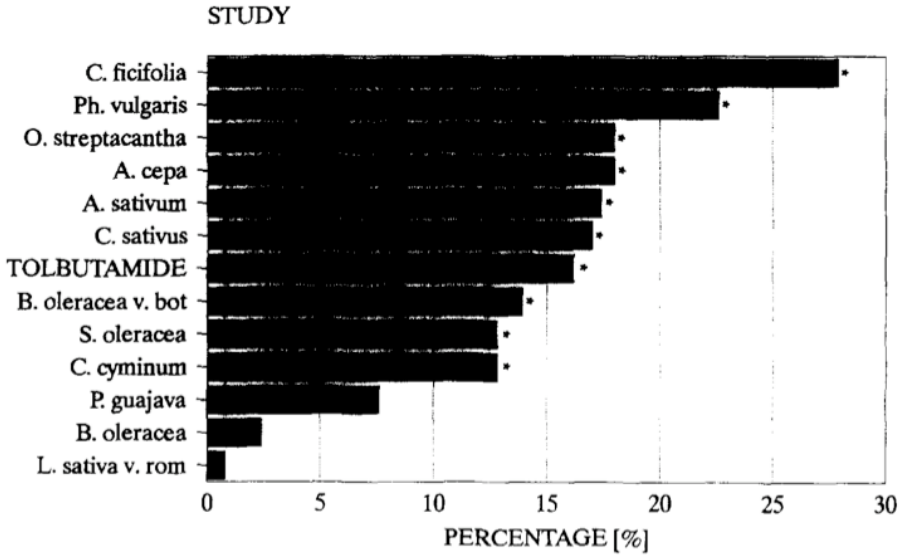


Fig. 2. Decrease in percentage of the hyperglycemic peak in healthy rabbits as compared to the water control (*$P < 0.05$).

Figure extracted from Roman-Ramos et al. 1995: Significant (P<0.01) decrease of the hyperglycaemic peak.

Table extracted from Pari et al. 2004: The fasting blood glucose and plasma insulin values.

TABLE 1. EFFECT OF PPET ON LEVELS OF BLOOD GLUCOSE AND PLASMA INSULIN IN NORMAL AND EXPERIMENTAL RATS

Group	*Fasting blood glucose (mg/dL)*	*Plasma insulin (μU/mL)*
1. Normal	80.30 ± 4.42[a]	14.60 ± 0.60[a]
2. Normal + PPEt	67.90 ± 3.77[a]	15.85 ± 0.69[b]
3. Diabetic control	278.54 ± 22.50[b]	4.00 ± 0.25[c]
4. Diabetic + PPEt	89.80 ± 3.40[c]	7.78 ± 0.40[d]
5. Diabetic + glibenclamide	97.60 ± 6.90[d]	7.06 ± 0.31[d]

Data are mean ± SD values from 10 rats in each group.
Values not sharing a common superscript letter differ significantly at $P < .05$ (DMRT). By the Duncan procedure, ranges for the level are: 2.91; 3.06; 3.16; 3.22.

Several *in vivo* studies were performed to investigate the influence of the *Phaseolus vulgaris* preparations on the blood glucose values.

One study used decocted green bean pods: 132 g of dried plant were boiled in 1 l water on slow heat for 10 minutes, cooled at room temperature and filtered (Roman-Ramos *et al.* 1995). The extract used by Pari *et al.* (2004) was prepared by extracting 132 g dried pods of *Phaseolus vulgaris* with 1 l water for 2 hours at 60-70°C. The extract was evaporated to dryness in a rotavapor at 40-50°C under reduced pressure. Normoglycaemic animals (rabbits, rats) as well as streptozotocin-treated hyperglycaemic rats were used. The groups of animals were sufficiently large for comparison. Fasting glucose levels as well as glucose tolerance was evaluated at several intervals.

The bean pod preparations reduced the hyperglycaemia and had a lowering effect on fasting blood glucose in hyperglycaemic rats. The doses used in the studies amounted to high levels (up to 500 mg extract per kg body weight), which makes extrapolation to human conditions difficult. However doses dependency can be considered as a positive fact.

Bean preparations

Reporting on the investigations with beans (Phaseoli fructus) and preparations thereof is out of scope of this assessment report. References on the investigations with bean extracts are included separately in the list of references (see *References not supporting the assessment report*).

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

No data available.

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

Toxicological data found in literature are on the beans (Phaseoli fructus) and cannot be extrapolated to bean pods (Phaseoli fructus sine semine).

3.4. Overall conclusions on non-clinical data

In vivo studies were performed with beans as well as with bean pod preparations. Rats (normal as well as hyperglycaemic and obese) and rabbits were used as animal species. Only outcomes related to bean

pods are presented in this assessment report. Bean pod preparations reduced the glycaemia and increased insulin activity. No dose-activity relationship was studied, as only single doses were used.

No non-clinical toxicity studies were done. As a consequence there are no data regarding genotoxicity, mutagenicity or teratogenicity for the herbal substance and preparations thereof. Nevertheless, bean pods can be considered as safe because of the composition and the long-standing use as a food substance.

4. Clinical Data

4.1. Clinical Pharmacology

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

A clinical trial with 18 healthy volunteers, aged 29 (±4.8) with a BMI of 23 (± 3.7) performed by Cerović *et al.* in 2006, showed no significant effects on glucose tolerance. The participants received either dry *Phaseolus vulgaris* extract from bean pods or placebo 30 minutes before a 50 g oral glucose tolerance test. Blood samples were drawn at 0, 15, 30, 60, 90 and 120 minutes.

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

No data available.

4.2. Clinical Efficacy

4.2.1. Dose response studies

No dose response studies available.

4.2.2. Clinical studies (case studies and clinical trials)

The only clinical studies available are investigations done with extracts of the beans (Phaseoli fructus) on weight reduction and hypoglycaemic effect as endpoints. However these data are out of scope for this assessment report.

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

No data available.

4.3. Overall conclusions on clinical pharmacology and efficacy

All clinical studies were performed with bean preparations instead of the traditionally used bean pods. As a consequence a possible therapeutic role for bean pods (Phaseoli fructus sine semine) is not supported by clinical evidence. The efficacy or pharmacological effects of the bean pods in the indication found in the monograph are plausible on the basis of long-standing use and experience.

5. Clinical Safety / Pharmacovigilance

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

No data available.

5.2. Patient exposure

No data available. As there are no constituents of concern in bean pods and there exists a long-standing use of the substance as a food, the use of the preparations thereof may be considered as safe.

5.3. Adverse events and serious adverse events and deaths

By lack of clinical studies, no clinical safety data were systematically collected. There are no other clinical toxicological data available. If contamination of bean pods with beans should occur, there might be a theoretical risk of adverse events caused by the beans. Therefore some adverse effects caused by beans are presented below.

One case of severe anaphylaxis to *Phaseolus vulgaris* has been reported. Ingestion of cooked kidney beans caused a systemic reaction by a 23-year-old woman having no atopic history. Half an hour later, the reaction resulted in an anaphylactic shock, which requested epinephrine and steroid treatment. Phaseolin and the lectin phytohaemagglutinin were identified as the putative allergens after skin prick tests and Western blotting (Rougé *et al.* 2011).

Inhalation of vapours from cooked white bean induced two episodes of angioedema in a seven-year-old boy having no allergic background. No problems occurred after previous contact with *Phaseolus vulgaris*. Next to skin prick and prick-by-prick tests, a determination of the serum IgE and an oral challenge test were performed. All tests were positive for *Phaseolus vulgaris* and negative for other legumes. The serum IgE against white and green bean amounted respectively 24.30 KU/l and 7.2 KU/l, with a total serum IgE of 230 KU/l (Martinez *et al.* 2005).

5.4. Laboratory findings

None reported.

5.5. Safety in special populations and situations

Interaction with oral hypoglycaemic drugs and insulin is possible due to the blood sugar level reducing effect. No studies on the effect of preparations from green bean pods during pregnancy and lactation have been performed. No investigations on handling machinery or driving vehicles were conducted.

5.6. Overall conclusions on clinical safety

No clinical data are available on toxicity of bean pods (Phaseoli fructus sine semine). Theoretically the concomitant use with antidiabetic drugs can result in an interaction. Patients using oral hypoglycaemic drugs and insulin may require further attention. Nevertheless, bean pods can be considered as safe because of the composition and the long history of use as a food substance.

6. Overall conclusions

Safety

No adverse reactions were reported with bean pods. Non-clinical and clinical toxicology, genotoxicity, mutagenicity or teratogenicity of bean pods were not investigated. Nevertheless, bean pods can be considered as safe because of the composition and the long history of use as a food substance.

No Community list entry can be established.

Efficacy

No clinical studies were done with the bean pods. Based upon historical reporting, a traditional use of bean pods (Phaseoli fructus sine semine) can be granted. This tradition points to the use as a mild diuretic.

The bean pods (Phaseoli fructus sine semine) can be considered as a traditional herbal medicinal product used to increase the amount of urine to achieve flushing of the urinary tract as an adjuvant in minor urinary tract complaints. The recommended posology is 2.5 g comminuted herbal substance in 150 ml of boiling water as a herbal infusion, to be taken 2 to 6 times per day.

Therapeutic area: 'Urinary tract and gynaecology disorders'.

Annex

List of references