Fructus Sennae

Definition

Fructus Sennae consists of the dried ripe fruit of *Cassia senna* L. (Fabaceae).[1]

Synonyms

Fabaceae are also referred to as Leguminosae.

Cassia acutifolia Delile and *Cassia angustifolia* Vahl. (*1*) are recognized as two distinct species in a number of pharmacopoeias as Alexandrian senna fruit and Tinnevelly senna fruit (*2–7*). Botanically, however, they are considered to be synonyms of the single species *Cassia senna* L. (*1*).

Selected vernacular names

Alexandria senna, Alexandrian senna, cassia, eshrid, falajin, fan xie ye, filaskon maka, hindisana, illesko, Indian senna, ma khaam khaek, makhaam khaek, Mecca senna, msahala, nelaponna, nelatangedu, nilavaka, nilavirai, nubia senna, rinji, sanai, sand hijazi, sanjerehi, sen de Alejandria, sen de la India, senna makki, senna, senna pod, senamikki, sona-mukhi, Tinnevelly senna, true senna (*8–11*).

Description

Low shrubs, up to 1.5 m high, with compound paripinnate leaves, having 3–7 pairs of leaflets, narrow or rounded, pale green to yellowish green. Flowers, tetracyclic, pentamerous and zygomorphic, have quincuncial calyx, a corolla of yellow petals with brown veins, imbricate ascendent prefloration, and a partially staminodial androeceum. The fresh fruit is a broadly elliptical, somewhat reniform, flattened, parchment-like, dehiscent pod, 4–7 cm long by 2 cm wide, with 6–10 seeds (*9*, *12*, *13*).

Plant material of interest: dried ripe fruit

General appearance

Fructus Sennae is leaf-like, has flat and thin pods, yellowish green to yellowish brown with a dark brown central area, oblong or reniform. Fruit is pale to greyish green, 3.5–6.0 cm in length, 1.4–1.8 cm in width; stylar point at one end,

[1] *Cassia italica* Mill. is listed in the Malian pharmacopoeia.

containing 6–10 obovate green to pale brown seeds with longitudinal prominent ridges on the testa (*2*).

Organoleptic properties

Colour is pale green to brown to greyish black (*2, 3*); odour, characteristic; taste, mucilaginous and then slightly bitter (*2*).

Microscopic characteristics

Epicarp with very thick cuticularized isodiametrical cells, occasional anomocytic or paracytic stomata, and very few unicellular and warty trichomes; hypodermis with collenchymatous cells; mesocarp with parenchymatous tissue containing a layer of calcium oxalate prisms; endocarp consisting of thick-walled fibre, mostly perpendicular to the longitudinal axis of the fruit, but the inner fibres running at an oblique angle or parallel to the longitudinal axis. Seeds, subepidermal layer of palisade cells with thick outer walls; the endosperm has polyhedral cells with mucilaginous walls (*2*).

Powdered plant material

Brown; epicarp with polygonal cells and a small number of conical warty trichomes and occasional anomocytic or paracytic stomata; fibres in two crossed layers accompanied by a crystal sheath of calcium oxalate prisms; characteristic palisade cells in the seeds and stratified cells in the endosperm; clusters and prisms of calcium oxalate (*4*).

Geographical distribution

The plant is indigenous to tropical Africa. It grows wild near the Nile river from Aswan to Kordofan, and in the Arabian peninsula, India, and Somalia (*12, 13*). It is cultivated in India, Pakistan, and the Sudan (*8, 9, 11–14*).

General identity tests

Macroscopic, microscopic, and microchemical examinations (*2–7*), and thin-layer chromatographic analysis for the presence of characteristic sennosides (sennosides A–D).

Purity tests

Microbiology

The test for *Salmonella* spp. in Fructus Sennae products should be negative. The maximum acceptable limits of other microorganisms are as follows (*15–17*). For preparation of decoction: aerobic bacteria—10^7/g; moulds and yeast—10^5/g; *Escherichia coli*—10^2/g; other enterobacteria—10^4/g. Preparations for internal use: aerobic bacteria—10^5/g or ml; moulds and yeast—10^4/g or ml; *Escherichia coli*—0/g or ml; other enterobacteria—10^3/g or ml.

Foreign organic matter

Not more than 1.0% (*2*).

Total ash

Not more than 6% (*3*).

Acid-insoluble ash

Not more than 2.0% (*2*, *4*, *5*).

Water-soluble extractive

Not less than 25% (*2*).

Moisture

Not more than 12% (*5*).

Pesticide residues

To be established in accordance with national requirements. Normally, the maximum residue limit of aldrin and dieldrin in Fructus Sennae is not more than 0.05 mg/kg (*17*). For other pesticides, see WHO guidelines on quality control methods for medicinal plants (*15*) and guidelines for predicting dietary intake of pesticide residues (*18*).

Heavy metals

Recommended lead and cadmium levels are not more than 10 and 0.3 mg/kg, respectively, in the final dosage form of the plant material (*15*).

Radioactive residues

For analysis of strontium-90, iodine-131, caesium-134, caesium-137, and plutonium-239, see WHO guidelines on quality control methods for medicinal plants (*15*).

Other purity tests

Chemical tests and tests of alcohol-soluble extractive to be established in accordance with national requirements.

Chemical assays

Contains not less than 2.2% of hydroxyanthracene glycosides, calculated as sennoside B (*2–7*). Quantitative analysis is performed by spectrophotometry (*2*, *5–7*) or by high-performance liquid chromatography (*19*).

The presence of sennosides A and B (*3–5*) can be determined by thin-layer chromatography.

Major chemical constituents

Fructus Sennae contains a family of hydroxyanthracene glycosides, the most plentiful of which are sennosides A and B (for structures, see page 244). There are also small amounts of aloe-emodin and rhein 8-glucosides, mucilage, flavonoids, and naphthalene precursors (*12*, *13*, *20*).

Dosage forms

Crude plant material, powder, oral infusion, and extracts (liquid or solid, standardized for content of sennosides A and B) (*12*, *20*, *21*). Package in well-closed containers protected from light and moisture (*2–7*).

Medicinal uses

Uses supported by clinical data

Short-term use in occasional constipation (*21–25*).

Uses described in pharmacopoeias and in traditional systems of medicine

None.

Uses described in folk medicine, not supported by experimental or clinical data

As an expectorant, a wound dressing, an antidysenteric, and a carminative agent; and for the treatment of gonorrhoea, skin diseases, dyspepsia, fever, and haemorrhoids (*11*, *23*, *25*).

Pharmacology

Experimental pharmacology

The effects of Fructus Sennae are due primarily to the hydroxyanthracene glucosides, especially sennosides A and B. These β-linked glucosides are secretagogues that induce net secretion of fluids, and specifically influence colonic motility and enhance colonic transit. They are not absorbed in the upper intestinal tract; they are converted by the bacteria of the large intestine into the active derivatives (rhein-anthrone). The mechanism of action is twofold: an effect on the motility of the large intestine (stimulation of peristaltic contractions and inhibition of local contractions), which accelerates colonic transit, thereby reducing fluid absorption; and an influence on fluid and electrolyte absorption and secretion by the colon (stimulation of mucus and active chloride secretion), which increases fluid secretion (*24*, *25*).

Clinical pharmacology

The time of action of Senna is usually 8–10 hours, and thus the dose should be taken at night (*24*). The action of the sennosides augments, without disrupting, the response to the physiological stimuli of food and physical activity (*24*). The

sennosides abolish the severe constipation of patients suffering from severe irritable bowel syndrome (*26*). In therapeutic doses, the sennosides do not disrupt the usual pattern of defecation times and markedly soften stools (*24*). Sennosides significantly increase the rate of colonic transit (*27*) and increase colonic peristalsis, which in turn increases both faecal weight and dry bacterial mass (*24, 28*). Due to their colonic specificity, the sennosides are poorly absorbed in the upper gastrointestinal tract (*29*).

Toxicity

The major symptoms of overdose are griping and severe diarrhoea with consequent losses of fluid and electrolytes. Treatment should be supportive with generous amounts of fluid. Electrolytes, particularly potassium, should be monitored, especially in children and the elderly.

Contraindications

As with other stimulant laxatives, the drug is contraindicated in cases of ileus, intestinal obstruction, stenosis, atony, undiagnosed abdominal symptoms, inflammatory colonopathies, appendicitis, abdominal pains of unknown cause, severe dehydration states with water and electrolyte depletion, or chronic constipation (*20, 21, 30*). Fructus Sennae should not be used in children under the age of 10 years.

Warnings

Stimulant laxative products should not be used when abdominal pain, nausea, or vomiting are present. Rectal bleeding or failure to have a bowel movement after use of a laxative may indicate a serious condition (*31*). Chronic abuse with diarrhoea and consequent fluid and electrolyte losses may cause dependence and need for increased dosages, disturbance of the water and electrolyte balance (e.g. hypokalaemia), atonic colon with impaired function and albuminuria and haematuria (*21, 32*).

The use of stimulant laxatives for more than 2 weeks requires medical supervision.

Chronic use may lead to pseudomelanosis coli (harmless).

Hypokalaemia may result in cardiac and neuromuscular dysfunction, especially if cardiac glycosides (digoxin), diuretics, corticosteroids, or liquorice root are taken (*29*).

Precautions

General

Use for more than 2 weeks requires medical attention (*21, 31*).

Drug interactions

Decreased intestinal transit time may reduce absorption of orally administered drugs (*32, 33*).

The increased loss of potassium may potentiate the effects of cardiotonic glycosides (digitalis, strophanthus). Existing hypokalaemia resulting from long-term laxative abuse can also potentiate the effects of antiarrhythmic drugs, such as quinidine, which affect potassium channels to change sinus rhythm. Simultaneous use with other drugs or herbs which induce hypokalaemia, such as thiazide diuretics, adrenocorticosteroids, or liquorice root, may exacerbate electrolyte imbalance (*20*, *21*).

Drug and laboratory test interactions

Urine discoloration by anthranoid metabolites may lead to false positive test results for urinary urobilinogen and for estrogens measured by the Kober procedure (*32*).

Carcinogenesis, mutagenesis, impairment of fertility

No *in vivo* genotoxic effects have been reported to date (*34–37*). Although chronic abuse of anthranoid-containing laxatives was hypothesized to play a role in colorectal cancer, no causal relationship between anthranoid laxative abuse and colorectal cancer has been demonstrated (*38–40*).

Pregnancy: non-teratogenic effects

Use during pregnancy should be limited to conditions in which changes in diet or fibre laxatives are not effective (*41*).

Nursing mothers

Use during breast-feeding is not recommended owing to insufficient available data on the excretion of metabolites in breast milk (*21*). Small amounts of active metabolites (rhein) are excreted into breast milk, but a laxative effect in breast-fed babies has not been reported (*21*).

Paediatric use

Contraindicated for children under 10 years of age (*21*).

Other precautions

No information available concerning teratogenic effects on pregnancy.

Adverse reactions

Senna may cause mild abdominal discomfort such as colic or griping (*21*, *22*, *33*). A single case of hepatitis has been described after chronic abuse (*42*). Melanosis coli, a condition which is characterized by pigment-loaded macrophages within the submucosa, may occur after long-term use. This condition is clinically harmless and disappears with cessation of treatment (*33*, *43*, *44*).

Long-term laxative abuse may lead to electrolyte disturbances (hypokalaemia, hypocalcaemia), metabolic acidosis or alkalosis, malabsorption,

weight loss, albuminuria, and haematuria (*21*, *22*, *33*). Weakness and orthostatic hypotension may be exacerbated in elderly patients who repeatedly use stimulant laxatives (*21*, *33*). Conflicting data exist on other toxic effects such as intestinal-neuronal damage after long-term misuse (*45–54*).

Posology

The correct individual dose is the smallest required to produce a comfortable, soft-formed motion (*21*). Powder, 1–2 g of fruit daily at bedtime (*8*, *19*, *20*). Adults and children over 10 years: standardized daily dose equivalent to 10–30 mg sennosides (calculated as sennoside B) taken at night.

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