



PHARMACOGNOSTICAL AND BIOLOGICAL STUDIES ON SENNA & ITS PRODUCTS: AN OVERVIEW

VIJAY AGARWAL*, MEENAKSHI BAJPAI

Department of Pharmacy, Rajkumar Goel Institute of Technology, 5-Km. Stone, Delhi-Meerut Road, Ghaziabad (U.P)-201003, India

Corresponding author

vagarwal5@rediffmail.com

ABSTRACT

Senna has been traditionally used as laxative by civilizations across the world. Leaflets are the primary parts used for medicinal purposes. Senna pods are also used for making sweetened decoctions for use as laxative. Senna leaflets contain sennosides as main phytoconstituents. The present article is aimed to provide a broad overview of quality control standards, pharmacology, clinical usage, patented & marketed formulations and global trade scenario for Senna and its products.

KEYWORDS

Senna, sennosides, laxative, standards.

INTRODUCTION

Herbal medicines and food supplement industry has seen quite phenomenal growth in the recent years. India has a wealth of flora with hundreds of the plants possessing medicinal or curative properties. Despite this wealth, India has a small share in medicinal plants trade in the world market. This dismal condition is attributable to several factors including non-identification of bioactive molecules, lack of uniformity in cultivation, processing, storage, transport, extraction and formulation processes.¹

Senna is one of the most commonly used laxative drugs in the Eastern and Western countries for the treatment of constipation. Commercially available consists of the dried leaflets of Alexandria senna (*Cassia acutifolia* Delile) or Tinnevely senna (*Cassia angustifolia* Vahl) belonging to plant family Leguminosae.^{2,3} Though perceived as two distinct species in several pharmacopoeias, they are now considered as single species i. e. *Cassia senna*.⁴

Senna is known for its purgative action. The phytoconstituents principally responsible for its characteristic action are two anthraquinone glycosides namely; sennoside A and sennoside B.

Sennoside A and B together are responsible for upto 40 – 60% activity of crude senna. Senna also contains small quantities of other anthraquinones such as sennosides C and D, rhein 8-glucoside, rhein-8-diglucoside, aloe-emodin, 8-glucoside, anthrone diglucoside and rhein. Additionally senna contains naphthalene glycosides (tinnevellin glycoside and 6-hydroxy musizin glycoside), flavonoid (kaempferol), phytosterols, myricyl alcohol, salicylic acid, chrysophenic acid, mucilage, resin and calcium oxalate.^{5,6}

Sennosides are not restricted to leaflets only; they are present in various vegetative and reproductive structures (underground as well as aerial). Maximum content of sennoside B is found in aerial parts. The distribution of sennoside B in *C. angustifolia* has been reported (Table 1).⁷

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Table 1.
Sennoside B content in various parts of C. angustifolia.

| Part | Sennoside B content (%) |
|----------------------|-------------------------|
| Filament and Anthers | 7.2 |
| Carpels and ovaries | 5.8 |
| Petals | 5.2 |
| Sepals | 4.7 |
| Flowers | 4.3 |
| Flower stalk | 3.2 |
| Leaflets | 2.8 |
| Pericarp | 2.4 |
| Stems | 0.2 |
| Roots | 0.05 |

Morphological, microscopical and organoleptic characters

The morphological, microscopical and organoleptic characters of senna have been determined. The qualitative and quantitative microscopy forms are one of the bases for the standardization of the drug.

Entire leaflets

The leaflets are characteristically lanceolate or lanceolate-ovate, with unequal base, entire margin and acute-mucronate apex. The leaflets have short and stout petioles which are sometimes broken. The leaflets are 1.5 – 6.0 cm long and 0.5 – 1.5 cm wide. They are pubescent with more number of appressed hairs on the lower surface than on the upper one. Some specific morphological features are also present in the leaves of *cassia angustifolia* and *cassia acutifolia*, which made them distinct from each other, as mentioned in table 2. The dried leaves available in commerce are weak yellow to pale olive in color. They have a characteristic odour and mucilage-like / slightly bitter taste.⁸

Table 2.
Distinct morphological characteristics of Cassia angustifolia and Cassia acutifolia

| Morphology | <i>Cassia angustifolia</i> | <i>Cassia acutifolia</i> |
|------------|------------------------------------|---|
| Appearance | Less entire and more broken | Entire and less broken |
| Size | 2-4 cm long, 7-12 mm wide | 2.5-6 cm long, 7-8 mm wide |
| Shape | Ovate-lanceolate | Lanceolate |
| Margin | Entire and curled | Entire |
| Apex | Acute with sharp spine at the apex | Less acute with sharp spine at the apex |
| Base | More asymmetrical | Less asymmetrical |
| Texture | Thin and brittle | Firm and flexible |
| Colour | Pale grayish-green | Pale green |
| Surface | More pubescent | Less pubescent |

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Microscopic examination of leaflets

Microscopic examination of the transverse section of senna leaflet reveals isobilateral structure. Paracytic stomata (**A**), nonlignified unicellular trichomes with warty walls (**B**) and fibrovascular bundle lined with abundant prisms of calcium oxalate (**C**) are characteristic features of senna leaflet.

Quantitative microscopy of leaflets has been undertaken and various parameter values have been reported (Table 3).^{4,9}

Table 3.
Quantitative microscopy standards for senna leaflet.

| Parameter | C. angustifolia | | C. acutifolia | |
|-------------------|-----------------|---------------|---------------|---------------|
| | Upper Surface | Lower surface | Upper Surface | Lower surface |
| Palisade ratio | 4.5-18 | 3.5-14.5 | 4-12 | 2.5-10.5 |
| Stomatal index | 10-15 | | 19.5-22.5 | |
| Vein islet number | 25-29.5 | | 19.5-22.5 | |

Powdered drug

Powdered senna has light green to greenish yellow color, characteristic odor and mucilaginous taste. Microscopic examination of the powder essentially reveals the presence of three characters **A**, **B** and **C** as in case of leaflet. **A** amongst polygonal epidermal cells, **B** isolated or attached to fragments of epidermis; and **C** are frequently visible in the powder. Cluster crystals appear isolated or in fragments of parenchyma.^{4,9}

Description and characterization of senna may be made with considering some parameters such as solubility, moisture content etc (table 4).¹⁰⁻¹²

Table 4.
Characteristics of senna powder

| Description | | Senna leaf |
|----------------------------------|------------|---|
| Solubility | Water | 1 in 35 of water |
| | Chloroform | 1 in 3700 Of chloroform |
| | Ether | 1 in 6100 of ether |
| | Alcohol | 1 in 2100 of alcohol |
| Category | | Stimulant purgative |
| Use | | In constipation |
| Organoleptic Properties | Odour | Slight |
| | Taste | First mucilaginous and sweet then slightly bitter |
| | Colour | Yellowish Green |
| Molecular formula of Sennoside B | | C ₄₂ H ₃₈ O ₂₀ |
| Molecular Weight of Sennoside B | | 862.7 |
| Moisture Content | | Sennoside should not contains more than 5% |



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General identity test

10.0 ml of ethanolic sodium hydroxide are added to 0.5 g of the powdered leaf and the resultant mixture is boiled on a water-bath. The volume of the extract is made upto 10.0 ml with water, and filtered. The filtrate is acidified with hydrochloric acid and extracted with 10.0 ml of ether. The ether layer is separated and shaken with 5.0 ml of ammonia; production of a yellowish red color in the ammonia layer confirms the identity of the drug.¹³

Purity tests

Microbiology

senna products should test negative for the presence of *Salmonella* sp.. The maximum permissible limits of microbes in senna products (decoctions and internal use preparations) have been described (Table 5).

Table 5.
Maximum permissible limits of microbes in senna products

| Microbe | Decoction | Internal Use preparation |
|----------------------|-----------|--------------------------|
| Salmonella | Nil | Nil |
| Aerobic bacteria | $10^7/g$ | $10^5/g$ |
| Mould and yeast | $10^5/g$ | $10^4/g$ |
| Escherichia coli | $10^2/g$ | Nil |
| Other enterobacteria | $10^4/g$ | $10^3/g$ |

Foreign Organic Matter

Not more than 2.0 % of stem and not more than 1.0 % of other foreign organic matter

Total Ash

Not more than 12.0 %

Acid Insoluble Ash

Not more than 2.0 %

Water Soluble Extractive

Not less than 3 %

Pesticide Residue

To be established in accordance with national requirements. Normally, the maximum residue limit of aldrin and dieldrin in senna is not more than 0.05 mg/kg.

Heavy Metals

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

Radioactive Residues

For analysis of strontium-90, iodine-131, caesium-134, caesium-137, and plutonium-239, WHO guideline on quality control describes the methods for medicinal plants.⁴

Substitutes and Adulterants

The leaves of the following plants have also been reported as mixed with or substituted for senna

1. *Cassia auriculata* (Palthe senna)- Leaves are small, oblong or obovate and conspicuously mucronate
2. *Cassia holoserica*- Leaves are smaller, more obtuse and hairy
3. *Cassia Montana*- Leaves are darker in colour, rounded apex and dark network of veins

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4. *Solenostemma argel* (Argel leaves)- Leaves are thick, rigid texture and peculiarly curled, curved, or twisted appearance, surface finely wrinkled, veins not evident, leaf equal at base and taste is distinctly bitter
5. *Tephrosia apollinea*- Leaves are obovate-oblong in shape, pubescent, emarginated, lateral veins straight and parallel
6. *Colutea arborescens* (Bladder senna)- Leaves are green and very thin
7. *Ailanthus glandulosa*- Leaves are large, triangular-ovate in shape, strongly striated cuticle and no stomata on upper epidermis
8. *Globularia alypum* (Province senna)- Leaves are spatulate, mucronate, rounded apex and prism of calcium oxalate present in the epidermal cells
9. *Coriaria myrtifolia*- Leaves are ovate-lanceolate in shape, grayish-green in colour, having two prominent lateral veins and conspicuous midrib.
10. *Cassia obovata* (Dog senna)- Leaves broadly obovate, apex abruptly tapering, pinnate venation.^{3,5}

PHARMACOLOGY OF SENNA

Experimental Pharmacology

Senna owes its characteristic pharmacological effects primarily to the presence of hydroxyanthracene glycosides viz. sennosides A and B. These glycosides increase secretion of gastric fluids and affect colonic motility and hence, facilitate colonic transit. These phytoconstituents remain unabsorbed in the upper intestinal tract. They are activated by large intestine bacteria into the active derivatives (rhein-anthrone).^{4, 14}

Clinical Pharmacology

Senna usually produces its characteristic action in 8-10 hours. Hence, its use at night is recommended. Sennosides relieve severe constipation. Normally, the sennosides do not alter the routine defecation time pattern and soften the stool. These chemical constituents result in increased colonic transit rate

and increased colonic peristalsis. This condition result in increased faecal weight and dry bacterial mass.^{4, 15}

Pharmacokinetics

Sennosides being β -o-linked glycosides remain unabsorbed in the upper gut and unaffected by digestive enzymes. Bacteria present in the large intestine convert these sennosides into the active metabolite – rheinanthrone is oxidized into rhein and sennidins. Orally administered sennosides are mainly excreted as polyquinones in faecal matter. Few metabolites are excreted in urine and bile while some senna metabolites such as rhein accumulate in breast milk.^{16- 18}

Overdosage & Adverse Drug Reactions

Overdose symptoms include griping and severe diarrhea with consequential loss of body fluids and electrolytes. Hypersensitive reactions such as pruritus, urticaria, local or generalized exanthema are very rare.

Chronic use; however; may cause alteration in water equilibrium and electrolyte metabolism. Chronic use has been found to cause pigmentation of the intestinal mucosa which recedes following the stoppage of Senna products consumption. Sometimes, albuminuria and haematuria may be observed. Red-brown or yellow discoloration of urine by senna metabolites may be noticed.

Long-term laxative abuse may result in weakness and orthostatic hypotension in elderly patients. There have been conflicting reports on effects such as intestinal-neuronal damage.^{19- 20}

Management of overdosage

Treatment is mainly supportive with a generous provision of fluid intake. Electrolytes (particularly potassium) need to be critically monitored in pediatric and geriatric populations.

Diarrhea may cause potassium depletion leading to cardiac disorders and muscular asthenia. The simultaneous use of cardiac glycosides,



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diuretics, adrenocorticosteroids and liquorice root must be avoided.

adrenocorticosteroids, or liquorice root may require constant medical supervision.

Contraindications

Senna products are contraindicated in the following populations:

1. Persons with ileus, intestinal obstruction, stenosis, atony, inflammatory colonopathies, appendicitis, severe dehydration states with water and electrolyte depletion.
2. Children below the age of 10 years.
3. Patient with known hypersensitivity to senna.
4. Patient using cardiac glycosides, antiarrhythmic medicinal products including QT-prolongation, diuretics, adrenocortico steroids or liquorice root.
5. Patients suffering from faecal impaction and undiagnosed, acute or persistent gastrointestinal complaints.

Drug Interactions

Senna products and its crude form also shows the interaction with some other drugs

1. Decreased intestinal transit time resulting from senna products consumption may interfere with absorption of orally administered drugs.
2. The increased potassium loss enhances the effect of cardiotonic glycosides (digitalis, stropanthus).
3. Existing hypokalaemia resulting from long term laxative abuse can also potentiate the affect of antiarrhythmic drugs, such as quinine, which affects potassium channels to change sinus rhythms.
4. Simultaneous use with other drugs or herbs such as thiazide diuretics,

Drug and laboratory test interactions

Anthranoid metabolites in may result in false positives for urinary urobilinogen and estrogens.

Carcinogenesis, Mutagenesis, Impairment of fertility

No *in vivo* genotoxic effects have been reported.

Pregnancy

Senna products usage must be avoided during the first trimester of pregnancy. Usage must be limited to the conditions where changes in diet or fibre laxatives are ineffective.

Nursing mother

Insufficiency of clinical data on metabolites excretion in breast milk necessitates avoidance of senna consumption wherever possible.¹⁸⁻²⁰

Chemical assays

Senna leaflets contain not less than 2.5% of hydroxyanthracene glycosides, calculated as sennoside-B. Thin-layer chromatography is used for detecting the presence of sennoside A and B. Quantification may be done by spectrophotometry, fluorometry and high-performance liquid chromatography.⁶

Posology

The correct individual dose is the smallest dose, required to produce a comfortable, soft-formed motion. Different senna products and their dose have been reported (Table 6).^{3, 19}

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Table 6.
Dosage of Senna and its products

| Product | Dose (Adult and children over 10 years) |
|--|--|
| Powder | 1-2 g of leaf daily dose at bedtime Standardized daily dose equivalent to 10-30 mg sennosides calculated as sennoside B |
| Dried leaf | 0.6–2.0 g |
| Infusion or decoction | 0.6–2.0 g in 150 ml hot water for 10 to 30 minutes |
| Cold macerate | 0.6–2.0 g in 150 ml cold water for 10 to 12 hours, strain, and then heat before drinking |
| Fluid extract 1: 1 (g/ml) | 0.6–2.0 ml |
| Elixir | 0.6–2.0 ml sweetened fluid extract |
| Dry hydroalcoholic extract (5.5–8.0% hydroxyanthracene glycosides) | 0.25–0.55 g |

Dosage forms

Senna and its products are commercially available in the following forms:

1. Senna powder
2. Senna granules
3. Senna fluid extract
4. Senna oral extract
5. Senna oral infusion
6. Senna syrup
7. Sennosides tablets

Some bulk forming and stimulant combination

Senna products are also available in combination with other drugs in selected national markets as exemplified below:

1. Psyllium and senna (Granules; U.S.)
2. Psyllium hydrophilic mucilloid and senna (Granules; Canada)
3. Psyllium hydrophilic mucilloid and sennosides (Powder; U.S.)

Patented formulations²¹

Certain patents have been granted for senna products based-formulations (Table 7).

Table 7.
Patented formulations

| Proprietary name | Holder of registration certificate | Active compound |
|------------------|------------------------------------|--------------------------|
| Ex-Lax senna | Novartis South Africa (PTY) Ltd. | Sennoside A and B 150 mg |



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| | | | |
|-----------------------------|----------|-------------------------|--------------------------|
| Ex-Lax senna chocolate | Novartis | South Africa (PTY) Ltd. | Sennoside A and B 150 mg |
| Reg-u-letts senna | Novartis | South Africa (PTY) Ltd. | Sennoside A and B 150 mg |
| Reg-u-letts senna chocolate | Novartis | South Africa (PTY) Ltd. | Sennoside A and B 150 mg |

Formulations in India

In India senna products have available in different dosage form (tablet, powder, syrup). Generic products and their company name also have been reported (Table 8).

Table 8.
Some formulations in india market

| Generic name | Company name | Dosage Form |
|------------------------|---------------------|-------------|
| Senade | Cipla Ltd | Tablet |
| Senasof | Wander Pvt.Ltd. | Tablet |
| Softovac powder | Lupin | Powder |
| Pursennid | Novartis | Tablet |
| Naturolax forte powder | Organon (India) Ltd | Powder |
| Ayurolax | Ajanta pharma Ltd | Tablet |
| Senalax | Cipla Ltd | Syrup |
| Laxatin | Alembic | Tablet |
| Laxsene | Alpine | Tablet |

Global Scenario

Calcium sennoside is a traditional product used as laxative. In recent times, Calcium sennoside is reported to be using its market share to natural fibre based products, which are considered to have less side effects.

Global supplier include the following

Interchem Corp., USA
Alcon-Couvreur NV, Belgium
Conforma, NV, Belgium
Jenssempharma A/S, Denmark
Brandeis Intestl France SA, France
Sunkyoung USA Inc., USA
PMC Specialities Group, USA

Growth rate and assessment of demand

As calcium sennoside is plant based drug and phytopharmaceutical and it is a traditional drug (used since 9th or 10th century) and it is produced in selected area in the world, including India, the product has been traditionally exported from India. The production level of calcium sennoside in India is about 180 tones per annum, out of which domestic Indian consumption level and export level are 40 and 140 tones per annum respectively. The annual growth rate in demand of calcium sennoside is 5-6% (domestic and export demand)

Growth Drivers

1. Increase awareness about adverse effect of synthetic drugs, has boosted up the demand of senna in domestic and export market.



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2. However, to sustain the global market share, special efforts by way of research and development and product application development has to be intimated for senna and its extract.
3. Senna extract and powder is comparatively cheaper than other synthetic drugs and formulations, used in constipation.
4. Herbal drugs have no adverse effect and are safe to use.
5. Senna project should be export oriented²².

CONCLUSION

Constipation is a global health problem. Diet and exercise are essential parts of the treatment of this problem, but use of traditional medicines, derived from plants, are the major form of treatment. In fact, the use of this kind of medicine still persists in many parts of world, especially in Asia. Senna is extensively cultivated in many parts of the world including India. Leaf and plant extract (calcium sennoside) of this plant has been used as an herbal medicine for the treatment of constipation. The purgative (stimulant purgative) action of *Cassia senna* has been extensively studied. Its morphological characteristics, mechanism of action, pharmacokinetics, adverse reactions, contraindications, drug interaction are well understood.

Senna and its products are commercially available in different dosage form (tablet, powder, syrup, extract, granules) with or without combination of other drugs. Different formulations of senna are available in global market, in which some patented also.

The global herbal market is estimated at US 60 billion dollars. China enjoys the lead, contributing 30% to the world market. The growth rate for herbal market is estimated to be around 7-15% annually. But growth rate of calcium sennoside is about 5-6% in India.

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