Egyptian Herbal Monograph

Volume 2

Pharmacopoeial wild medicinal plants

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***Senna alexandrina* Mill.** سنا مكي

1. Names & Synonyms (1-3)

***Senna alexandrina* Mill.**

Family: Leguminosae (Caesalpinioideae).

Syns.: *Cassia acutifolia* Delile, *Cassia senna* L., *Cassia lanceolata* Forssk.

Arabic: Sanna Mekki سنا مكى , Salamekki سلامكى.

English: True Senna, Alexandrian Senna.

2. Geographical distribution

The Nile region, desert east of the Nile including that of Sinai as well as the Red Sea and Gebel Elba regions (3).

3. Parts used for medicinal purposes

Leaves and pods (3).

4. Major chemical constituents

- **Anthraquinones**: Sennosides A and B, sennosides C and D (4), gluco aloe-emodin, rhein-8-monoglucoside, rhein 8-diglucoside, sennidin (5-7).
- **Naphthalene glucoside:** 6-Hydroxymusicin glucoside (8).
- **Flavonoids:** Mostly as mono- and di-*O*-glycosides of quercetin, kaempferol and isorhamnetin (5).

5. Medicinal uses

Well-established uses

A. Purgative (9) for short term use in occasional constipation (10).

Traditional medicinal uses

B. Stimulant laxative (11).

***S. alexandrina* is a traditional medicinal plant for use in the specified indications exclusively based upon long-standing use.**

6. Herbal preparation correlated to medicinal use

1. Liquid extract (alcoholic 30%) (12).
2. Infusion (13).
3. Decoction, dried extract, elixir, granules (pharmaceutical), oral solution, powder, rectal suppositories and tablets (14-15).
4. The boiled tea of leaves, sweetened with black honey, is taken in the morning before breakfast for treatment of constipation (11).

7. Posology and method of administration correlated to medicinal use

Adult oral dose:

- **Powdered drug:** 0.5-3gm (12).
- **Liquid extract:** 0.5-3ml (12).
- **Senna preparations expressed in terms of total sennosides calculated as sennoside B:** The usual adult dose is 15 to 30 mg given by mouth once or twice daily (15).

Children younger than 12 years of age: under medical supervision (14).

- Children over 6 years of age: one-half the adult dose (15).
- Children aged 2 to 6 years: one-quarter the adult dose (15).
- Not to be used by children younger than 2 years of age (15).

Elderly patients: Should initially take half of the normal prescribing dose (13).

8. Contraindications

- Hypersensitivity to active substances and to other plants of the same family.
- Children younger than 2 years of age (13).
- It should not be used by persons with intestinal obstruction, ulcerative colitis, gastrointestinal bleeding, appendicitis, nausea, vomiting, congestive heart failure, or an acute condition in the abdomen caused by surgery (14).
- Patients with suspected stricture, inflammatory bowel disease, or impending obstruction should not receive a bowel stimulant, to reduce the risk of colonic perforation (15).
- Senna should not be given to patients with undiagnosed abdominal pain (15).
- Prolonged use should generally be avoided (15).

9. Special warnings and precautions for use

- If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.
- Hypersensitivity reactions manifesting as asthma and rhinoconjunctivitis have been reported in those manufacturing or dispensing Senna products (15).
- It should not be used for longer than 1-2 weeks without medical advice (14).
- Children younger than 12 years of age should not be used unless prescribed by a physician (14).

10. Interactions with other medicinal products and other forms of interaction (14)

- Cardiac glycosides (digoxin): Chronic use of Senna may potentiate cardiac glycosides.
- Disulfiram: Do not use Senna with disulfiram.
- Laxatives /stimulant laxative herbs: Avoid the concurrent use of Senna with other laxatives; additive effect can occur.
- Jimson weed (*Datura stramonium* L.): The action of Jimson weed is increased in cases of chronic use or abuse of Senna.

11. Fertility, pregnancy and lactation

- The use of Senna should be avoided during pregnancy (13) and lactation due to its content of anthraquinones (16) which is distributed into breast milk (15).
- No fertility data available.

12. Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed.

13. Undesirable effects

- If adverse reactions occur, a doctor or a pharmacist should be consulted.
- Senna may cause mild abdominal discomfort such as colic or cramps (15), nausea, vomiting, anorexia, cramping, diarrhea, flatulence, hypocalcemia, enteropathy, alkalosis and hypokalemia (14).

14. Overdose

- Prolonged use or over dosage can result in diarrhoea with excessive loss of water and electrolytes, particularly potassium; there is also the possibility of developing an atonic non-functioning colon. Anthraquinone derivatives may colour the urine yellowish-brown at acid pH, and red at alkaline pH. Reversible melanosis coli has been reported following chronic use (15).
- Prolonged use or abuse of Senna laxatives has been associated with reversible finger clubbing, hypokalaemia and tetany, hypertrophic osteoarthropathy, intermittent urinary excretion of aspartylglucosamine, hypogammaglobulinaemia, reversible cachexia, and hepatitis or hepatic failure (15).

15. Relevant biological activities

-The laxative action and the laxative potency of Alaxandria and Tinnevelley senna in mice were studied using a standardized procedure. The results indicated that the laxative potency of various grades have been found to be reasonably uniform, the variations in potency not exceeding 25 per cent of the mean (17-18).

- The effect of repeated administration of the doses of Alexandria or Tinnevelly senna on mice over many weeks were studied. Two sets of experiments were conducted. In the first set of experiments no tolerance to either Tinnevelly or Alexandria senna developed. In the second set of experiments, 31 out of 40 mice survived the twenty-three-week period. It would therefore seem that mice may be used once a week for quantitative assay of laxative activity of senna and the repeated administration of the doses over many weeks did not cause any tolerance (19).

-Intravenous and intraperitoneal injections of Senna infusion produced negligible cathartic response compared to the same dose after oral administration (20).

- The effect of repeated administration of the doses of Alexandria Senna on mice over many weeks was studied. It would therefore seem that mice may be used once a week for quantitative assay of laxative activity of Senna and the repeated administration of the doses over many weeks did not cause any tolerance (19).

-Purgative action of Senna depends on the amount of hydroxyanthraquinone existing in the plant (21-22) but the effect is not due to the presence of sennoside A and B only (23), rather a synergistic action of different components (24), because Senna extracts are more potent laxatives than the pure active principles (25). Oral Senna-pod extract reverses net absorption of water, sodium and chloride to net secretion, and increases potassium secretion and stimulates output of PGE2 into the colonic lumen (26). The purgative action of Senna has been attributed, in part, to the release of histamine in the gut (27).

- Senna extract (SE) causes diarrhea and enhances gastrointestinal motility through digestive tract administration. Long-term gastric administration of SE induces inflammatory changes and cell damage in the whole gastrointestinal tract. The differential proteins screened from the colonic tissues of the model mice might mediate the enhancing effect of SE on gastrointestinal motility (28).

16. Additional information

Senna preparations may be used for bowel evacuation before investigational procedures or surgery, prior to X-ray examination or in mechanical preparation in the evening before elective colonic or rectal resection, as a colon cleansing, for elective colonoscopy (15, 29-32).

- The *β-O*-linked glycosides (e.g. sennosides and rhein 8-*O*-glucoside) are neither absorbed in the upper gut nor split by human digestive enzymes. They are converted by the bacteria of the large intestine into the ultimately active metabolite (rheinanthrone) (10, 33). The Aglycones are absorbed in the upper gut.

- Animal experiments with radio-labeled rheinanthrone administered directly into the caecum demonstrated absorption < 10%. In contact with oxygen, rheinanthrone is oxidised into rhein and sennidins, which can be found in the blood, mainly in the form of glucuronides and sulphates.

- After oral administration of sennosides, 3 - 6% of the metabolites are excreted in urine; some are excreted in bile (10). However, most of the sennosides (ca. 90%) are excreted in faeces as polymers (polyquinones) together with 2 - 6% of unchanged sennosides, sennidins, rheinanthrone and rhein. (10.)

- In human pharmacokinetic studies with Senna pods powder (20 mg sennosides), administered orally for 7 days, a maximum concentration of 100 ng rhein/ml was found in the blood, but an accumulation of rhein in blood was not observed. Small amounts of rhein pass into breast milk (10).

- Animal experiments demonstrated that placental passage of rhein is low.

17. Date of compilation/last revision

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References

1	Boulos, L. (2000). Flora of Egypt, Al Hadara Publishing, Cairo, Egypt.
2	Batanouny, K. H. (1999). Wild Medicinal Plants in Egypt. (with contribution: Aboutabl, E., Shabana, M. and Soliman, F.). Academy of Scientific Research and Technology, Egypt. The World Conservation Union (IUCN).
3	Hassan, N. M. and Abdelmohsen, M. M. (2020). *Senna alexandrina* Mill. In: Egyptian Encyclopedia of Wild Medicinal Plants, **9**, 473-480. Academy of Scientific Research and Technology, Cairo, Egypt.
4	Dave, H. and Ledwani, L. (2012). A review on anthraquinones isolated from Cassia species and their applications. *Indian Journal of Natural Products and Resources*, **3**(3), 291-319.
5	Farag, M. A., Porzel, A., Mahrous, E. A., El-Massry, M. M. and Wessjohann, L. A. (2015). Integrated comparative metabolite profiling via MS and NMR techniques for Senna drug quality control analysis. *Anal. Bioanal. Chem.*, **407**, 1937–1949. https://doi.org/10.1007/s00216-014-8432-1.
6	Agarwal, V. and Bajpai, M. (2010). Pharmacognostical and biological studies on *Senna* and its products: An overview. *International Journal of Pharma and Bio Sciences*, **6**(2), 1-10.
7	Rastogi, R. P. and Mehrotra, B. N. (1990). Compendium of Indian Medicinal Plants, Publication and Information Directorate, CSIR, New Delhi, **1**, 81-83.
8	Franz, G. (1993). The senna drug and its chemistry. *Pharmacology*, **47**(1), 2-6. doi: 10.1159/000139654. PMID: 8234429.
9	Egyptian Pharmacopoeia (2005). 4th edition. General Organization for Government Printing. Cairo.
10	European Union Herbal Monograph on *Senna alexandrina* Mill. (*Cassia senna* L.; *Cassia angustifolia* Vahl), fructus (2018). EMA/HMPC/228761/2016. Committee on Herbal Medicinal Products (HMPC).
11	Conservation and Sustainable Use of Medicinal Plants in Egypt, National Surveys (2016). UNDP, GEF, ASRT and NRC, volumes 1-5.
12	Egyptian Pharmacopoeia (1972). 2nd edition. General Organization for Government Printing. Cairo.
13	PDR for Herbal Medicines (1998). Medical Economic Co. Montvale, New Jersey, 639. ISBN 1563633612, 9781563633614.
14	Skidmore-Roth (2010). Mosby's Handbook of Herbs and Natural Supplements. St. Louis: Mosby, 4th ed. ISBN: 978-0-323-05741-7.
15	Martindale: The Complete Drug Reference (2007). Pharmaceutical Press. Electronic version, London.
16	Joint Formulary Committee (2008) British National Formulary. 55th ed., London: British Medical Association and Royal Pharmaceutical Society of Great Britain.
17	Grote, I.W. and Woods, M. (1944). Laxative action in mice of Tinnevelley and *Alexandria senna*, and of several botanically related plants. *J. Am. Pharm. Assoc. (Sci. edi),* **33**, 266–270.
18	Grote, I. W. and Woods, M. (1951). The laxative activity in mice of the various parts of the *Senna* plant. *J. Am. Pharm. Assoc*., **40**, 52–53.

19	Woods, M. and Grote, I.W. (1951). The repeated administration of Tinnevelly and Alexandria senna to mice. *J Am Pharm Assoc. (Sci. edi.)*, **40**, 198–202.
20	Hazleton, L. W. and Talbert, K. D. (1945). Factors influenceing the cathartic activity of *Senna* in mice. *J. Am. Pharm. Assoc. (Sci. edi)*, **34**, 260–264.
21	Auterhoff, H. (1953). Anthraquinone. III. The pharmacological action of anthraquinone derivatives. *Arzneimittel-Forsch*., **3**, 23–25.
22	Caravaggi, A. and Manfredi, A. (1937). Laxative action of active principles extracted from some commonly used plants. *Boll. Chim. Farm.*, **76**, 117–123.
23	Fairbairn, J. W. and Saleh, M. R. I. (1951). Vegetable purgatives containing anthracene derivatives. V. A third active glycoside of *Senna*. *J. Pharm. Pharmacol.*, **3**, 918–925.
24	Ploss, E. (1975). Synergism and potassium substitution as preferences in vegetable laxatives. *Dtsch. Apoth. -Ztg.,* **28**, 336–338.
25	Marvola, M., Koponen, A., Hiltunen, R. and Hieltala, P. (1981). The effect of raw material purity on the acute toxicity and laxative effect of sennosides. *J. Pharm. Pharmacol.*, **33**, 108–109.
26	Beubler, E. and Kollar, G. (1985). Stimulation of PGE2 synthesis and water and electrolyte secretion by *Senna* anthraquinones is inhibited by indomethacin. *J. Pharm. Pharmacol.*, **37**, 248–251.
27	Erspamer, E. and Paolini, A. (1946). Histamine a positive conditioner of the purgative action of some drastic agents. *Experientia*, **2**, 455–458.
28	Wang, X., Zhong, Y.X. and Lan, M. (2002). Screening and identification of proteins mediating Senna-induced gastrointestinal motility enhancement in mouse colon. *World J. Gastroenterol.*, **8**, 162–167.
29	Sitiris G. (1970). A new laxative, X-preparation: to be used as a bowel evacuant prior to X-ray examination. *Tidsskr Nor Laegeforen*, **90**, 1477–1478.
30	Shavakhi, A., Kianinia, M., Torabi, G., Nemati, A., Saeidian, B., Hoseinzadeh, M., Madjlesi, F., Navaei, P., Rashidinejad, F. and Minakari, M. (2011). High dose Senna or polyethylene glycol (PEG) for elective colonoscopy preparation: a prospective randomized investigator-blinded clinical trial. *J. Res. Med. Sci.*, **16**(2), 149–155.
31	Arezzo, A. (2000). Prospective Randomized Trial Comparing Bowel Cleaning Preparations for Colonoscopy. *Surg. Laparosc. Endosc. Percutan. Tech.*, **10**(4), 215-217.
32	Valverd, A., Hay, J., Fingerhut, A., Boudet, A., Petroni, R., Pouliquen, X., Msika, S. and Flamant, Y. (1999). Senna *vs* polyethylene glycol for mechanical preparation the evening before elective colonic or rectal resection. A multicenter controlled trial. *Arch. Surg.*, **134**(5), 514-519. doi:10.1001/archsurg.134.5.514.
33	Meselhy, R. M., Nishimoto, E., Akao, T. and Hattori M. (2001). Human intestinal Bacteroides spp. RHEIN-I and RHEIN-II capable of transforming rhein to rheinanthrone, induce rhein-dependent diarrhea in rats. *J. Trad. Med*. **18**, 169-176.