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Analytical evaluation of various tablets containing sennosides focusing on disintegration time and dissolution

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Abstract
Calcium sennosides A and B extracted from *Cassia angustifolia* has been used as stimulant laxative in herbal medicine. It has got medicinal value, hence is to be monitored and administered in appropriate dosage form. In this study attempts were made to analyse tablet formulations containing sennosides as the only active ingredient, as well as sennosides in combination with other purgatives. The study focuses on dissolution profile, disintegration time along with analytical evaluation as per the established monograph requirement like description, disintegration time, average weight, LOD, residue on ignition, pH, microbial evaluation, HPTLC fingerprinting, Assay - Content of sennosides A and B by Fluorometry. Also additionally tested for content of tannins, calcium, and iron. Dissolution profile was made for all samples. In-house single ingredient senna tablet preparation with lowest DT and appreciable dissolution can be considered as ideal laxative. Presence of calcium sennosides can give very good laxative effect.

Keywords: Analytical evaluation, tablet formulation, Sennosides, Dissolution, Laxative

1. Introduction
In today's competitive world where everyone is exposed to a fierce and continuous struggle for existence, due to changes in the lifestyle, often related to today's hectic pace of life, our food habits, overexertion, insufficient rest, intake of unhealthy diet especially one without enough fibres leads to the fairly common and uncomfortable complaint, called "Constipation". It usually involves difficult or irregular bowel movements, accompanied by hard, dry motion, which can be painful to pass. Senna works by gently stimulating the bowel to encourage bowel movement for relief from occasional or nonpersistent constipation. Leaves of senna [1] are astringent, bitter, sweet, acrid, thermogenic, cathartic, depurative, liver tonic, anthelmintic, cholagogue, expectorant and febrifuge, and are useful in constipation, abdominal disorders, leprosy, skin diseases, leucoderma, splenomegaly, hepatopathy, jaundice, helminthiasis, dyspepsia, cough, bronchitis, typhoid fever, anaemia, tumours and vitiated conditions of pitta and vata.

Senna leaf [2] is one of the most frequently employed botanical laxative remedies; it is counted among laxatives with hydragogue and anti-absorptive action. The drug is used for acute constipation and in all cases in which defecation with a soft stool is advisable, such as with hemorrhoids, after surgical interventions in the rectum or anal area, before and after abdominal operations, with anal fissures, for the evacuation of x-ray contrast media from the intestines, etc. The mechanism of action of the sennosides is relatively well understood; they first demonstrate their activity through an interaction with the intestinal bacteria, by which they are hydrolyzed and then reduced to the anthrone stage as the actual active form. The sennosides and other anthraquinone derivatives possess a laxative effect. Sennosides specifically influence large intestinal motility. Acceleration of colonic transport seems to be a major component of the laxative action. Anthraquinone works by irritating the lining of the upper intestine which provokes reflux muscular activity in the colon resulting in a bowel motion. Hence senna is considered as a powerful cathartic used in the treatment of constipation, working through a stimulation of intestinal peristalsis.

There are a large number of laxative products in the market. The dose of laxatives will be different for different products. The number of capsules or tablets or teaspoonfuls of crystals, gel, granules, liquid or powder we use, the number of caramels or wafers we eat or the number of pieces of gum that we chew depends on the strength of the medicine.

The active purgative principle was discovered [3] in 1866. It is a glucoside of weak acid character, and was named Cathartic Acid. Standardized senna extracts, containing about 20% sennosides, have an approximately 30% stronger laxative effect than the equivalent amount of pure sennosides because other accompanying constituents in the extract potentiate the effect. Over dosage can lead to colic-like intestinal pains and the discharge of thinly liquid stools. Senna leaf should not be used in cases of chronic constipation.

It is essential to monitor and quantify the sennoside content in the recommended dosage.

In the raw state senna contains a variable quantity of the active ingredients. However, the sennoside content of the senna used in the manufacture of senna tablet is standardized to ensure the constant desired amount of active ingredient and predictable result from every dose. Also most of the times the API used for preparation of senna tablets is the calcium salt of sennosides known as calcium sennosides. At the same time if excipients like dicalcium phosphate (DCP), calcium carbonate ($CaCO_3$) are used during the tablet preparation, then one has to quantify the total calcium content in the formulation.

Hence quality determination can be done on the basis of appropriate strength and physical status of the tablet formulation. Total seven tablet formulations were subjected to analytical evaluation – five single ingredient and two multi-ingredients. All these tablet formulations were subjected to the known official monograph requirements like description, average weight, disintegration time, dissolution, loss on drying (LOD), residue on ignition (Ash), pH, Assay – Content of sennosides A and B, HPTLC fingerprinting. Also these tablets were additionally evaluated for tannin content, calcium content, iron content, microbiological load and dissolution profile. Through this researchers are attempting to give additional test parameters for value addition in quality determination of the formulation.

2. Materials and Methods

2.1 Samples

Out of five single ingredient tablets containing sennosides A and B - the only active ingredient, sample number 1, 2, 3 were purchased from the local market, where as sample number 4 and 5 were prepared in our own laboratory – Inhouse preparation. Sample number 6 and 7 were multi-ingredient market samples where senna extract was supported with other ingredients like Triphala, Shiva, Castor oil.

2.2 Chemicals and Reagents

All the chemicals and reagents used in different processes were procured from M/s Merk India and M/s Qualigens.

2.3 Equipments and Instruments

All the glass-wares used were well calibrated and were procured from M/s Borosil Glass Works Ltd.

Instruments used were weighing balance (M/s Schimadzu Corporation), Electric oven (M/s Pathak Electrical Works Ltd.), pH meter (M/s Control dynamic Lab.), Disintegration Machine (M/s Thermonik), UV-visible spectrophotometer (M/s Schimadzu), HPTLC (M/s Anchrome and Camag Ltd.), Fluorometer (M/s Tecan Austria GmbH, Model safire II – BASIC), Dissolution apparatus (M/s Lab India Disso 2000).

2.4 Methods

Description, disintegration time, average weight, loss on drying, residue on ignition, HPTLC fingerprinting, assay – content of sennosides A and B by fluorometry and dissolution were carried out as mentioned in the USP monograph.[4]

Tannins were evaluated by titration method [5]. Calcium content by complexometry [6], and Iron content by spectrophotometric method [7]. Microbial testing was carried out as per USP and BP guidelines. Dissolution profile was carried out on the basis of assay mentioned in USP.

3. Results and Discussions

Physicochemical test parameters are reported in table 1.1 as per the standard pharmacopoeia.

Table 1.1: Physicochemical Test parameters in Tablet Formulations containing Sennosides

Spl No.	Description (color of the tablet)	Disintegration time (DT) in min.	Average weight in mg	Loss On Drying (LOD)at 105 ^{0}C in %w/w	Residue on Ignition (Ash) %w/w	pH of 1%w/v solution	Content of Sennosides A and B by Fluorometry in mg/tablet
1	Brown circular tablets	15	195.20	7.109	14.023	8.66	11.329
2	Brown circular tablets	18	193.00	5.791	13.841	8.73	10.059
3	Light Brown circular tablets	9	722.70	4.118	10.886	9.31	0.527
4	Light brown convex tablets	2	257.20	5.539	4.760	7.72	12.108
5	Light brown convex tablets	2	252.80	4.317	33.340	7.37	9.429
6	Dark brown circular tablets	20	624.56	7.369	16.422	6.46	30.102
7	Dark brown circular tablets	20	639.02	8.020	16.110	6.35	36.047

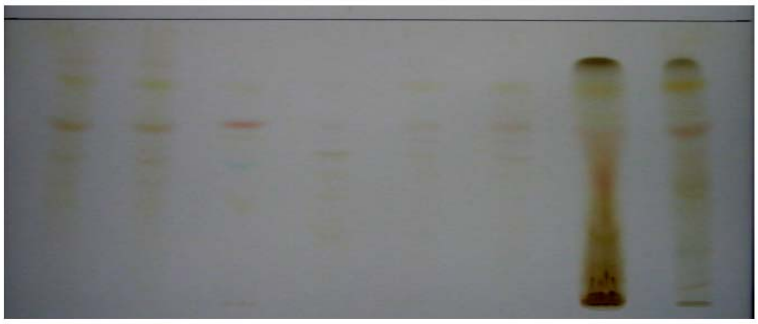
Disintegration time of in-house single ingredient tablet samples 4 and 5 are recorded to be 2 minutes, rest other showed variation from 9 minutes to 20 minutes. Variation observed in the average weight was from 193mg to 722 mg. Moisture in the form of LOD was ranging from 4.00%w/w to 8.00%w/w, whereas residue on ignition that is ash content was showing lot of variation from 4.76%w/w to 33.34%w/w with respect to the amount of inorganic elements present in the sample. pH of all single ingredient tablets was found to be above 7.00, the same was around 6.5 in both the multi

ingredient formulations. Data recorded in Table 1.2 assures the safety with respect to the microbial load in all samples.

Table 1.2: Microbiological evaluation of Tablet Formulations containing Sennosides

Sr. No	Test Parameters	Spl 1	Spl 2	Spl 3	Spl 4	Spl 5	Spl 6	Spl 7
i)	Total Aerobic Microbial Count in cfu/g	40	40	80	100	110	660	640
ii)	Total Combined Yeast /Moulds Count in cfu/g	<10	<10	<10	<10	<10	<10	<10
iii)	Bile-Tolerant Gram Negative Bacteria in cfu/g	<10	<10	<10	<10	<10	<10	<10
iv)	*Escherichia coli*	Absent	Absent	Absent	Absent	Absent	Absent	Absent
v)	*Salmonellae spp.*	Absent	Absent	Absent	Absent	Absent	Absent	Absent
vi)	*Staphylococcus aureus*	Absent	Absent	Absent	Absent	Absent	Absent	Absent
vii)	*Pseudomonas aeruginosa*	Absent	Absent	Absent	Absent	Absent	Absent	Absent
viii)	*Clostridium spp.*	Absent	Absent	Absent	Absent	Absent	Absent	Absent

Cfu/g: Colony forming unit per gram.



1 2 3 Std 4 5 6 7

Fig 1: HPTLC Fingerprinting profile of tablets containing sennosides

As shown in figure 1, HPTLC fingerprinting carried out as per guidelines given in the monograph from USP showed yellowish orange colored spots at Rf 0.72 and 0.84 after exposing the plate to ammonium hydroxide vapors. Assay of sennosides A and B was analysed on fluorometer and recorded in Table 1.1. Sample No. 3 showed the lowest value – 0.527 mg/tablet and sample number 4 showed the highest one around 12.108 mg/tablet amongst all single ingredient tablet formulations. Sennosides content in sample number 6 and 7 were 30.102 mg/tablet and 36.047mg/tablet respectively. Additional test parameters are recorded in Table 2.

Table 2: Additional Test Parameters in Tablet Formulation containing Sennosides

Spl No.	Residue On Ignition (Ash) in %w/w	Content of Tannins in %w/w	Content of Calcium	Content of Iron
1	14.023	2.869	3.653% = 7.130 mg/tab	1293.42 ppm = 0.252 mg/tab
2	13.841	3.213	3.893% = 7.513 mg/tab	1204.77 ppm = 0.232 mg/tab
3	10.886	2.537	0.404% = 2.919 mg/tab	459.02 ppm = 0.332 mg/tab
4	4.760	1.891	1.535% = 3.948 mg/tab	264.02 ppm = 0.067 mg/tab
5	33.340	1.814	10.340% = 26.139 mg/tab	239.41 ppm = 0.060 mg/tab
6	16.422	7.883	4.859% = 30.347 mg/tab	260.00 ppm = 0.162 mg/tab
7	16.110	8.119	5.037% = 32.187 mg/tab	240.00 ppm = 0.153 mg/tab

Tannins were found to vary between 1.814%w/w to 3.213% w/w in sample number 1 to 5, whereas, in sample number 6 and 7 tannins were found to be around 8%w/w due to the presence of additional sources of tannins like triphala, shiva in the multi ingredients tablet formulations. Since sennosides extract used was in the form of its calcium salt, attempts were made to monitor the content of calcium. Sample number 4 and 5 were in house formulations, where in sample number 5 calcium content was found to be more 26.139 mg/tablet compared to sample number 4 where it was 3.948 mg/tablet because of presence of additional component such as dicalcium phosphate (DCP) in the formulation 5. The reflection of which could be seen in the corresponding ash values too. The involvement of Ca^{2+} in the mechanism of the purgative action of rhein anthrone was studied [8]. Iron content was recorded in the range from 239.41 ppm to 1293.42 ppm.

Due to the high solubility of anthraquinone glycosides in water, dissolution profile of tablet formulations could add value to achieve the effect of medicament. El-hasan *et al* [9] studied the disintegration and dissolution rate and predicted that the harder the tablet the longer is its dissolution time. Dissolution profile up to 2 hours for tablets containing only Ca-sennosides is recorded in Table 3.1,

Table 3.1: Dissolution Profile of Single ingredient Tablet containing Sennosides

			ASSAY – Content of Sennosides A and B in mg / tablet							
Sample number	**DT in mins.**	**Assay (mg/tab)**	**2 mins.**	**5 mins.**	**10 mins.**	**15 mins.**	**30 mins.**	**60 mins.**	**90 mins.**	**120 mins.**
1	15	11.329	2.124	2.213	2.248	5.096	9.491	10.324	10.550	11.192
2	18	10.059	0.526	1.721	2.003	5.376	9.122	9.138	9.508	9.841
3	9	0.527	0.043	0.072	0.202	0.480	0.481	0.484	0.484	0.491
4	2	12.108	7.227	11.121	11.149	11.350	11.357	11.398	11.400	11.401
5	2	9.429	6.084	8.400	8.430	9.017	9.019	9.022	9.042	9.239

Whereas, dissolution profile up to 4 hours is recorded in Table 3.2

Table 3.2 Dissolution Profile of Multi-Ingredient Tablet containing Sennosides

			ASSAY – Content of Sennosides Aand B in mg / tablet									
Spl No.	**DT In min.**	**Assay (mg/tab)**	**5 mins**	**10 mins**	**15 mins**	**18 mins**	**20 mins**	**22 mins**	**25 mins**	**30 mins**	**60 mins**	**120 mins**
6	20	30.102	3.316	3.884	5.864	8.144	8.244	8.831	10.186	10.742	12.103	24.282
7	20	36.047	2.862	3.431	4.811	6.230	6.256	7.303	7.981	10.690	14.825	29.612

Table 3.2: Dissolution Profile of Multi-Ingredient Tablet containing Sennosides

Sample	**DT in min.**	**Assay (mg/tab)**	**135 mins**	**150 mins**	**180 mins**	**195 mins**	**210 mins**	**240 mins**
6	20	30.102	24.284	25.338	25.675	25.686	27.255	29.903
7	20	36.047	29.912	29.996	30.999	32.289	32.439	33.452

Single ingredient tablets showed almost more or equal to 90% dissolution after 2 hours. Sample number 1, 2, 3 with disintegration time 15, 18 and 9 minutes respectively showed dissolution about 19.84%, 19.91% and 38.33% of actual content after 10 minutes and 44.98%, 53.44% and 91.08% after 15 minutes respectively. In case of in-house preparations, sample number 4 and 5 where the disintegration time was recorded to be the lowest that is about 2 minutes, dissolution was found to be 92.07% and 89.40% after 10 minutes and 93.73% and 95.63% after 15 minutes in corresponding samples. In multi-ingredient tablet formulations dissolution of sennosides was found to be 12.90%, 9.51% after 10 minutes and 19.48%, 13.34% after 15 minutes. After 2 hours it was found to be 80.66%, 82.15% and after 4 hours 99%, 93% in sample number 7 and 8 respectively. However in multi-ingredient tablets ingredients used other than sennosides also contribute to the laxative effect and act as purgatives. Dissolution profile with respect to corresponding disintegration time of tablet samples under study is well illustrated in figure 2.

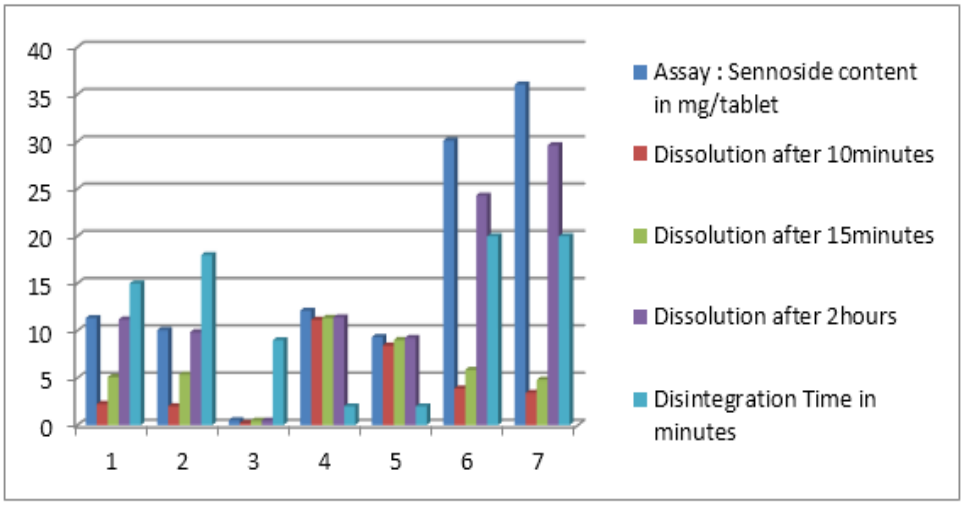


Fig 2: Dissolution Profile with respect to Disintegration Time
X axis →Sample Numbers
Y axis → Sennoside content in mg/tablet

Momin *et al* [10] in their study proved that calcium sennosides and senna extract tablet shows better dissolution than senna powder tablet.

Cassia angustifolia extract can be used as enema after abdominal operation. It regulates disordered function of gastrointestinal tract abdominal operations [11].

4. Conclusion

Additional test parameters can add value to the quality determination of tablet formulations. Dissolution profile of tablets containing only sennosides as active ingredient was found to be better than the multi-ingredient laxative formulations. In-house tablet preparations with lowest disintegration time showed appreciable dissolution. Analytical test parameters additionally proposed herewith, along with those proposed in the standard monograph listed in the pharmacopoeia assures the quality of the tablets containing sennosides.

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