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Formulation and evaluation of enteric coated tablet of Senna for the treatment of constipation

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Abstract
The plant based herbal formulations has captured the global market of medicines and herbal drugs in raw form now a day's moved to mainstream by thousands of people for the various health problems, because of the herbal drugs are free from side effects as compare to allopathic drugs available in the market. Therefore the use of traditional system of medicines increasing all over the world and other aspect is the growth of concerned pharmaceutical companies due to increasing the research process for the better quality, safety and efficacy. Senna is the most common stimulant laxatives used as active ingredient. This ingredient has been choice of researchers and ample scientific data is available on the same. Senna is official in various pharmacopoeias and also covered by world health organization (WHO) in its monograph on medicinal plants. Sennosides are the active chemical constituents of senna which is used for the relief of constipation. The pharmacological action of the sennosides is well known which act upon the large intestine and initial convey their action through an interaction with the intestinal bacteria, by which they are hydrolyzed and then reduced to the anthrone the actual active form. The sennosides specifically influence large intestinal motility. Acceleration of colonic transport seems to be a major component of the laxative action. The antraquinone glycosides work by irritating the lining of the upper intestine which incites reflux muscular activity in the colon resulting in bowel motion. Hence senna is considered as powerful laxative used in the treatment of constipation, working through a stimulation of intestinal peristalsis. This supports their pharmacological action in intestine, not in the stomach. Therefore, to make sure the entire quantity of drug is made available to intestine an attempt is made to formulate and evaluate the enteric coated tablet of senna. To achieve the enteric coated formulation Cellulose acetate phthalate was used as enteric coating material in different %age and *in vitro* release studies of senna tablet was carried out in 0.1 N HCl and Phosphate buffer pH6.8. It was observed during the studies that cellulose acetate Phthalate alone was sufficient to protect the senna tablet in stomach Environment.

Keywords: Enteric coated tablet, Senna, Cellulose Acetate Phthalate, Ajowan

Introduction
Senna is one of the most frequently employed botanical laxative remedies and well recognized drug used in the allopathic and Ayurvedic system of medicine. The laxative effect of senna is due to the presence of sennoside A & B. The drug is used for acute constipation and in all cases, in which defecation with a soft stool is advisable, such as with hemorrhoid, surgical interventions of rectum. The pharmacological action of the sennosides is well known; which act upon the large intestine and initial convey their action through an interaction with the intestinal bacteria, by which they are hydrolyzed and then reduced to the anthrone the actual active form. The sennosides specifically influence large intestinal motility. Acceleration of colonic transport seems to be a major component of the laxative action. Antraquinone glycoside work by irritating the lining of the upper intestine which incites reflux muscular activity in the colon resulting in a bowel motion. The bulky and softer fecal mass is produced due to the decrease in the water absorption in the intestine also. Hence senna is considered as powerful laxative used in the treatment of constipation, working through a stimulation of intestinal peristalsis. This evidences their pharmacological action in intestine, not in the stomach. Therefore, to make sure the entire quantity of drug is made available to intestine by preparing the enteric coated tablet of senna.
There are various factors which are essential for oral drug delivery system and solubility of drugs is the one of the important factor. The tablet of water soluble drug may release a significant amount of drug from the surface in physiological environment of stomach before reaching at the site of action. Senna are water soluble drug, hence an attempt was made to inhibit the drug release in the acidic environment of stomach and to ensure total drug release in

the intestine by enteric coating of senna tablet using cellulose acetate phthalate.

During present study, enteric coated tablets of senna extract and ajowan oil was successfully formulated by using cellulose acetate phthalate coating materials and could be completely averted initial loss of sennosides in stomach for the treatment of constipation. Some of the important observations of present work are as follows:

Material and Methods

The cellulose acetate phthalate polymer was gifted from Belco Pharma Bahadurgarh, Haryana the Propylene Glycol, Sorbitane monooleate (SPAN-80) and acetone was taken from Molychem, Mumbai, ethyl alcohol was taken from ADS spirits Haryana and senna extract was gifted by natural remedies, Bangalore, Karnataka, Ajowan oil was taken from Rama Pharmaceutical. Other excipients such as Microcrystalline cellulose (MCC) (PH 101), Microcrystalline cellulose (MCC) (PH 102) (Rama Pharmaceuticals), Pre-gelatinised starch, (Colorcon Ltd), β-cyclodextrin (Gangwal Chemical Ltd), Croscarmellose sodium (DVM), calcium carbonate (Sukkan India Ltd), Polyvinyl pyrrolidone (PVP) (ISP), Talc (J.B Pharma), Magnesium Stearate (S. Kant Healthcare) and Aerosil (Degussa) were used.

Steps used in the Formulation Development

There are four main steps used for the development of enteric coated tablet of senna.

- Encapsulation of Ajowan Oil
- Granulation of Senna Extract
- Formulation of Tablet
- Enteric Coated formulation

Formulation of Enteric Coated Tablet

Preparation of Enteric Coating Solution

The enteric coating solutions were prepared by using Cellulose acetate phthalate (CAP) in different concentration such 4%, 8%, 12%, 16%, 20% and 24%. The cellulose acetate phthalate (CAP) was dissolved in ethyl alcohol, sorbiton mono-oleate and part of acetone. To make sure appropriate spreading, the dye, titanium dioxide and talc were appropriately dispersed in acetone. After that the color solution was added to the coating solution.

Table 1: Formula for Enteric Coating Solution.

S. No	Ingredients (%)	ECT [1]	ECT [2]	ECT [3]	ECT [4]	ECT[5]	ECT [6]	ECT[7]
1.	Cellulose acetate phthalate	4	8	12	16	18	20	24
2.	Propylene Glycol	4	4	4	4	4	4	4
3.	Ethyl alcohol	40	40	40	40	40	40	40
4.	Sorbiton mono- oleate (span-80)	1.5	1.5	1.5	1.5	1.5	1.5	1.5
5.	Dye (Neelicol Ponceau 4R)	1	1	1	1	1	1	1
6.	Talc	1	1	1	1	1	1	1
7.	Titanium oxide	1	1	1	1	1	1	1
8.	Acetone	q. s to 100%	q. s to 100%	q. s to 100%	q. s to 100%	q. s to 100%	q. s to 100%	q. s to 100%

Enteric Coating Process

The enteric coating of optimized batch of senna tablet was done by conventional rotating pan using different concentration of cellulose acetate phthalate. The required amount of the coating solution was sprayed on pre-warmed tablet bed in a pan coater. The tablets are dried with the help of inlet air having temperature 40 °C to 50 °C. The coating process is repeated till the desired level of coating was achieved.

Tablet 2: Trail batch of different % of Cellulose Acetate Phthalate.

Trial Batch Excipients (mg)	$RCSA_1$	$RCSA_2$	$RCSA_3$	$RCSA_4$	$RCSA_5$	$RCSA_6$
Cellulose acetate phthalate	24	48	72	96	120	144
Senna Extract	150	150	150	150	150	150
Ajowan oil	36	36	36	36	36	36
β-cyclodextrin	64	64	64	64	64	64
MCC (PH101)	135	111	87	63	39	15
Cross carmelose sodium	35	35	35	35	35	35
MCC (PH 102)	14	14	14	14	14	14
PVP	40	40	40	40	40	40
Calcium carbonate	20	20	20	20	20	20
Pre-gelatinised starch	60	60	60	60	60	60
Talc	9	9	9	9	9	9
Magnesium stearate	9	9	9	9	9	9
Aerosil	4	4	4	4	4	4
Total Weight in (Mg)	600	600	600	600	600	600

Results and Discussion

Standard Plot of Senna in 0.1 N HCl

The plot of different concentration of senna in 0.1 N HCl vs. Absorbance was found to be linear in the concentration range of 4-24 µg/ml.

Table 3: Concentration versus Absorbance reading of senna in 0.1N HCl λ_{max} 276

S. No	Concentration (µg/ml)	Absorbance
1.	4	0.230
2	8	0.332
3	12	0.515
4	16	0.652
5	20	0.802
6	24	0.952

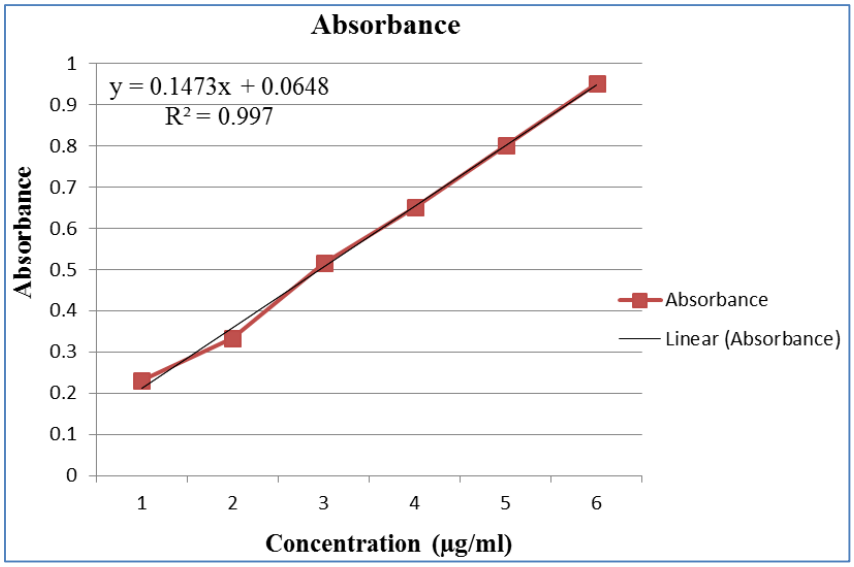

Fig 1: Celebrative curve of Senna in 0.1 N HCl

Table 4: Effect of different % of Cellulose Acetate Phthalate on disintegration time in different disintegration media.

Parameters	4% CAP containing tablet	8% CAP containing tablet	12% CAP containing tablet	16% CAP containing tablet	20% CAP containing tablet	24% CAP containing tablet
Disintegration time in 0.1 N HCl	Disintegrate	disintegrate	Unchanged after 2hrs	Unchanged after 2hrs	Unchanged after 2hrs	Unchanged after 2hrs
Disintegration time in phosphate buffer having pH 6.8	50 minutes 55 seconds	59 minutes 15 seconds	76 minutes 50 seconds	90 minutes 10 seconds	108 minutes 25 seconds	124 minutes 20 seconds

Table 5: Characteristics of senna tablets after enteric coating.

Parameters	4% CAP containing tablet	8% CAP containing tablet	12% CAP containing tablet	16% CAP containing tablet	20% CAP containing tablet	24%CAP containing tablet
Disintegration time	50 minutes 55 seconds	59 minutes 15 seconds	76 minutes 50 seconds	90 minutes 10 seconds	108 minutes 25 seconds	124 minutes 20 seconds
% drug release after 2 hrs	97.9	86.5	65.6	56.4	48.8	39.2
Drug contents	127%	114%	96%	85%	78%	55%

Table 6: percentage CDR.

Time (Hr)	% CDR					
	4% CAP containing tablet	8% CAP containing tablet	12%CAP containing tablet	16% CAP containing tablet	20% CAP containing tablet	24% CAP containing tablet
0.5	30.2	24.1	15.2	7.2	1.5	0.3
1.0	52.7	50.2	36.5	21.3	9.7	1.8
1.5	76.5	68.8	52.5	40.2	28.3	18.2
2.0	97.9	86.5	65.6	56.4	48.8	39.2
2.5		98.3	76.7	67.8	59.2	50.5
3.0		104.7	89.5	73.3	69.9	58.7
3.5			98.7	81.5	80.2	67.3
4.0				90.7	91.1	78.8

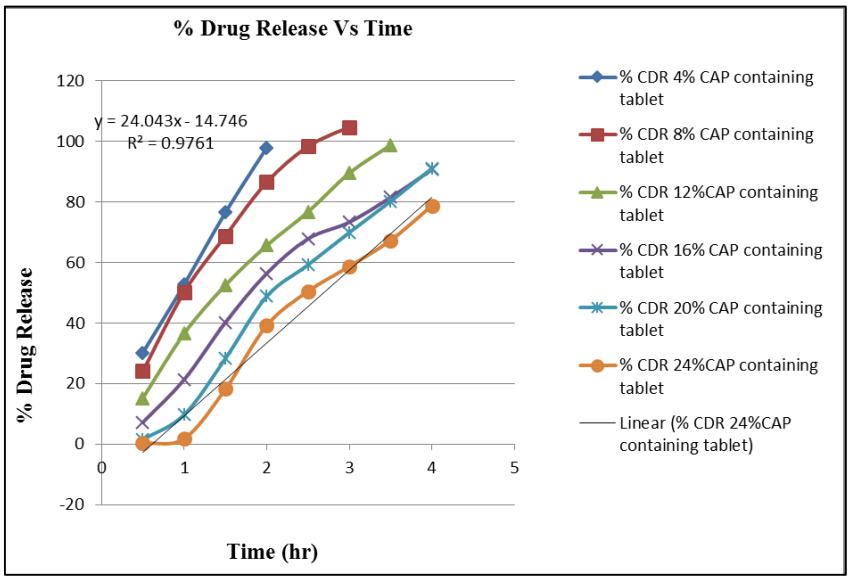

Fig 2: Cumulative graphe of % Drug release

Summary

Senna is one of the most frequently employed botanical laxative remedies and well recognised drug used in the allopathic and ayurvedic system of medicine. The laxative effect of senna is due to the presence of sennoside A & B. The drug is used for acute constipation and in all cases in which defecation with a soft stool is adivisable, such as with hemorrhoid, surgical interventions of rectum. The pharmacological action of the sennosides is well known; which act upon the large intestine and initial convey their action thruogh an interaction with the intestinal bacteria, by which they are hydrolyzed and then reduced to the anthrone the actual active form. The sennosides specifically influence large intestinal motility. Acceleration of colonic transport seens to be a major component of the laxative action. Antraquinone glycoside work by irritating the lining of the upper intestine which incites reflux muscular activity in the colon resulting in a bowel motion. The bulky and softer fecal mass is produced due to the decrease in the water absorption in the intestine also. Hence senna is considered as powerful laxative used in the treatment of constipation, working through a stimulation of intestinal peristalsis. This evidences their pharmacological action in intestine, not in the stomach. Therefore, to make sure the entire quantity of drug is made available to intestine by preparing the enteric coated tablet of senna.

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During present study, enteric coated tablets of senna extract and ajowan oil was successfully formulated by using cellulose acetate phthalate coating materials and could be completely averted intial loss of sennosides in stomach for the treatment of constipation.

The inlet temperature of enteric coating process was optimized by taking different temperature ranging from 30-70 °C. But the efficient enteric coating temperature was optimized between 40-50 °C. The six batches of drug were coated using different concentration (4%, 8%, 12%, 16%, 20% & 24%). The ethyl alcohol and acetone non aqueous solvents were used in the enteric coating system. The non aqueous system is suited to coating the drugs that are sensitive to water and heat. To produce good film characteristics the propylene glycol was used as plasticizer in coating system. The studies revealed that 12% cellulose acetate phthalate when used as enteric coating material give better results. The tablets that were coated with 4% cellulose acetate phthalate and 8% cellulose acetate phthalate solution do not pass the disintegration test. The disintegration time of the senna tablet was increased after enteric coating from 26 minutes to 76 minute and was released approximately 100% of drugs before and after enteric coating. The development of enteric coated formulation has been one approach to preventing the drug from coming into contact with gastric mucosa. The enteric coating dosage form releases the drug after leaving the stomach. The % of Cellulose acetate phthalate was optimized for gastric resistance because enteric polymer remains intact in stomach but release the drug content once it reaches the intestine. The results of this study indicate that enteric coated tablets using 12% CAP are suitable for the senna drug which is mainly active in the lower Gastro intestinal track. The different trail batches of enteric coated tablets were developed by using different % of cellulose acetate phthalate and drug release profile of different batches were studies with the help of five kinetic models namely Zero order, first order, higuchi, Hixon-crowell and Korsmeyer-Peppas model.

Future prospective

There is a scope to still further expand this work to minimize the overages of ajowan oil in order to reduce losses during processing. This makes the product more economical and cost effective.

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