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CONSTAC A IMPROVED LAXATIVE FOR CONSTIPATION: STABILITY STUDY

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ABSTRACT

Constipation is a symptom found in many individuals around the world and in clinical setting they visit very frequently. Prevalence of constipation is at around 2% to 28% in general community in all the ages. Availability of many therapies involks such individual to go with safest, standardized available treatment like allopathy. Ayurvedic drug which were tested as per standard like stability testing assures the identity, potency and purity of ingredients, as well as those of the formulated products. This stability study was conducted for constac granules as per CCRAS guidelines that is ensuring two years shelf life of this formulation for stable efficacy and quality.

KEYWORDS:

INTRODUCTION

Constipation is a symptom found in many individuals around the world and in clinical setting they visit very frequently. Prevalence of constipation is at around 2% to 28% in general community in all the ages.[1,2,3] Constipation is now routine terminology discussed in society and perception include subjective feeling of inability to pass feces easily, painful hard stool or obstruction while passing, urge for defecation but no satisfaction after defecation. Such perceptions makes it difficult for common definition of constipation in Indian population. Geographically normal frequency of defecation, stool forms, ethic factors, and food habits

also varies in the population.[4] Due to availability of multiple therapies, increased educational standards of living, individuals looks for more safe option to get relief from such symptom. In India major part of population use allopathic medications due to safety concern, comparative study says Ayurvedic and homeopathy drugs gives adverse events in nearby ration of 94:3.4:2.6.[5] Stability studies for longer duration generally include real time studies. In this study using CCRAS guidelines stability study of constac granules were conducted to ensure its shelf life. Shelf of product ensures that the efficacy and product quality remain unchanged in that specific period and can be considered as expired after it.

AIM AND OBJECTIVE

1. To evaluate organoleptic, physicochemical parameters and microbial load using real time stability study for constac powder a polyherbal formulation.

MATERIALS AND METHODS

1. Hirada (Fruit) Terminalia chebula[6]
2. Behada (Fruit) Terminalia bellirica[7]
3. Amala (Fruit) Emblica officinalis[8]
4. Isabgol (Husk) Plantago ovata[9]
5. Balhirada (Fruit) Terminalia chebula[6]
6. Sonamukhi (Leaves) Cassia Senna[10]
7. Mulethi (Root) Glycyrrhiza glabra[11]
8. Ajwain (Seed) Ptychotis ajowan[12]
9. Badishep (Fruit) Foeniculum vulgare[13]
10. Elaichi (Fruit) Elettaria cardamomum[14]
11. Erand Tail (Oil) Ricinus communis[15]
12. Narikel lavan (Processed salt with coconut)[16]
13. Permitted Preservatives and excipients q.s.

Storage condition and evaluation parameters

Real-time stability study successfully conducted[17] as per CCRAS guidelines over a period of 26 months in stability chamber. Carefully, changes in formulation were noted for 24 months at an interval of 1st, 6th, 12th, 18th and 24th months in maintained in recommended temperature of 30^{0}C±2^{0}C with, recommended relative humidity: 60% RH ±5^{0}C in stability chamber. Observations were analyzed, interpreted and prepared a report in next one month. 10% degradation was set as acceptable point.

List of parameters checked during the study

1. Organoleptic characters
2. Physico-chemical parameters
3. Microbial Load

- **Examination of color, odour and taste**

Color: Observation was done in bright background with light using 5gm powder. It was carefully observed by naked eyes as brown color granules.

Odor: Before smelling coffee beans were used to remove all previous odours. Churna taken in between thumb and 1st finger and smelled it and found it as Characteristic.

Taste: Churna taken in a spoon and tasted it on the tongue and examined for the type of taste and found it as bitter and salty.

Particle Size: 25g of the constac granules were placed in a sieve of suitable nominal mesh aperture. It was Shake in the sieve for not less than 30minutes in a rotatory horizontal direction and vertically by tapping on a hard surface. Weight was accurately calculated by the amount of remaining granules on the sieve and in the receiving pan.

- **Determination of loss on drying**

In dried petridish 2gm weighed constac powder were taken and placed it in an oven at 105-110^{0}C. Two consecutive times this cycle was repeated using two different petridish. After losing moisture content in powder it was weighed in digital balanced weighing machine. The weight after drying was noted and loss on drying was calculated for 1, 6, 12, 18, 24 month and found as 4.91%, 5.12%, 5.65%, 5.85% and 5.96% respectively for each month (Table 1).

- **Determination of pH**

1gm Constac granules were weighed in digital balanced weighing machine and mixed in 100ml of distilled water in volumetric flask. This 100ml solution was sonicated for about 10min. pH of this solution was calculated using digital pH meter. It was measured at 1st day of 1st month and after 1, 6, 12, 18 and 24 months which was found as 4.05, 4.02, 4.43, 4.45, 4.55 respectively for each month (Table 1).

➢ **Determination of total ash**

Constac granules air dried 1gm were weighed in digital balanced weighing machine were taken as sample. Gradually it was heated up to 500-600^{0}C this powder in muffle furnace till found it as carbon free. After cooling it in desiccators same is been placed in balanced weighing machine. Total ash content was calculated and expressed as % w/w of air dried material[18]. It was successfully calculated for 1st, 6th, 12th, 18th, 24th month and found as 2.80%, 2.85%, 3.12%, 3.35%, and 3.56% respectively for each month(Table 1).

➢ **Acid insoluble ash value**

After determining total ash it was poured in 250ml beaker without any loss of ash added 100 ml of dil. Hydrochloric acid in it. Using water bath this solution were boiled for 5 minutes followed by filtration of the solution and collected the insoluble matter on a ashless filter paper (whatmann no.41). This filtrate has been washed with hot water till get the neutral filtrate. Transferred this filter paper containing insoluble matter to the original crucible and dried on a hot plate at 600^{0}C using ignition in a muffle furnace (until it becomes white ash). Allowed this residue to cool in suitable desiccators for about 30 minutes and weigh without delay. Repeated the process until constant weight obtained. Calculated this acid insoluble ash with reference to the air dried drug for 1st , 6th , 12th , 18th , 24th month which was found 0.68% for 1st and,6th month which was decreased to 0.67% in 12th.18th and 24th month (Table -1).

➢ **Water soluble ash value**

Ash obtained from the total ash determination procedure boiled for 5 minutes with 25ml of water. In a gooch crucible carefully collected insoluble matter on an ash less filter paper. Using hot water washed it and ignited it for 15 minutes at a temperature not exceeding 600^{0}C. Subtracted the weight of the insoluble matter from the weight of the ash, the difference in weight represent the water soluble ash. Calculated the percentage of water soluble ash with reference to the air dried for 1st, 6th, 12th, 18th, 24th months found as 1.36%, 1.35%, 1.37%, 1.38%, and 1.40% respectively for each month (Table-1).

➢ **Determination of water soluble extractive value**

Air dried constac granules were 5 gm weighed in digital balanced weighing machine. These granules macerated in glass stoppered conical flask in which 100ml chloroform water were added and again macerate it for 6hrs. It was shaked frequently and once stopped allow it to stand for 18hrs. Rapidly filtered it after 24hrs and 20ml of filtrate was transferred in a tarred

flat bottom evaporating dish with a pipette and placed above boiling water to evaporate it to dryness. Again evaporating dish dried at 105^0C for 6hrs in oven. After cooling weight of this residue was noted and percentage of water soluble extractive was calculated and expressed as % w/w 18with reference to dried air sample for 1st, 6th, 12th, 18th and 24th month was found as 53%, 51%, 49%, 49% and 47% respectively for each month.

- **Determination of alcohol soluble extractive value**

Constac granules weighed 5g macerated with 100 ml of alcohol of specified strength in a closed flask for 24 hours, it has been shaked frequently for 6 hours than allowed to stand for 18 hours. This solution were filtered rapidly taking precautions for loss of solvent. Evaporated 25ml of the filtrate to dryness in tared flat bottom shallow dish and dried at 105^0C to constant weight. Calculated the percentage of alcohol- soluble extractives with reference to the air-dried drug for 1st,6th, 12th, 18th, and 24th months was found as 18%, 16%, 14%, 13% and 13% respectively for each month.

- **Estimation of bitter residue**

Air dried constac granules were weighed 1 gm in digital balanced weighing machine, poured it to 150ml conical flask and mixed it with 50ml of methanol. In water bath it was refluxed for half an hour. Methanol extract was collected after filtration in 250ml of beaker. This residue again extracted similarly 2 times and total 3 methanol extracts were separated and evaporate it to obtained 5ml volume thick paste. Using 25 ml hot water in three cycles shake it till water soluble matter is extracted or dissolved. Separate this water washed extracts and pour it to separating funnel. Using 25ml of petroleum ether (60-80^0C) with minimum 4 cycles aqueous extract was extracted. This extract of petroleum ether was washed using 25 ml ethyl acetate and repeated 3 more cycles of ethyl acetate extraction. This extract then separated and transferred to pre-weighed evaporating dish and after evaporation dry residue were obtained. From the weight of the residue, the percentage of bitter residue was calculated and expressed as % w/w with reference to air dried sample[19] which was found as 3.72% on day 1^{st} of 1^{st} month, 3.64% at 6 months, 3.29% at 12 months, 3.20% at 18 months and 3.15% at 24 months (Table-1).

- **Estimation of Total Saponin**

Air dried constac granules were 5gm weighed in digital balanced weighing machine taken into the conical flask. 50ml of 90%v/v methanol were added, and refluxed it for half an hour. Once the cooling done it was filtered and residue was washed with 90%v/v methanol till get a

colorless extract. On water bath combined methanol extract evaporated and thick paste like residue obtained. This residue treated by using 25 ml petroleum ether (60-80^{0}C) than separated the layer of petroleum ether. Residue than treated with 25ml chloroforms and separated it also. Using ethyl acetate 25 ml residues treated and then layer of ethyl acetate separated. 90%v/v methanol in volume of 5 ml added to this residue and mixed well till residue dissolved completely. This solution poured into beaker containing 25 ml acetone drop by drop with constant stirring to obtain precipitate. Flask rinsed using 90%v/v methanol (about 2ml). Decant the organic layer and residue to constant weight. The percentage of total saponin was calculated and expressed as % w/w with reference to air dried sample[19] which was found as 3.1% on day 1st, 2.8% at 6th months, 2.8% 12th months, 2.7% at 18th months, 3.4% at 24th months.

- **Estimation of Total Tannin: For blank, For sample**

For blank: In 500 ml conical flask 300ml distilled water and 25 ml indigo sulphonic acid solution added and mixed well. This solution than titrated against 0.02M KMnO4 solution till stable golden yellow colored developed and burette reading was noted.

For sample: Air dried constac granules were weighed 0.05gm in digital balanced weighing machine. This sample poured in 500ml conical flask and 50ml distilled water added to it till the sample dissolves completely. In this solution 250ml distilled water carefully added and again mixed well. This solution sonicated for 10min and 25ml indigo sulphonic acid solution was added and mixed well. Carefully titrated this solution against 0.02M KMnO4 solution till get stable golden yellow color. The burette reading was noted. The percentage of total tannin was calculated using following factor. 1 mL of 0.02M KMnO4 is equivalent to 0.00415g of tannin substance[20] which was observed at 1st, 6th, 12th, 18th, 24th month as 26%, 25%, 25.55%, 25.60% and 24% respectively.

Microbial load

As per Indian pharmacopeia[18] standards microbial load calculated in which bacterial count, total fungal count, presence of Escherichia coli, Salmonella spices, Pseudomonas aeruginosa and Staphylococcus aureus were calculated which was found as absent during the study period. Pure culture was obtained from NCIM pune and media used for microbial limit test were HiMedia Pvt. Ltd.

RESULTS

This real time stability study performed in temperature 30^0C±2 C, relative humidity 60%RH±5% which was maintained till 24th month during the study. Product was analyzed from 1st day of 1st month, 6, 12, 18, till 24th month. No change was observed over a period of 24 months as summarized in table No-1.

Real time stability study parameters of constac granules-table 1

Sr. No	Parameters	Observations				
		1st Year studies		2nd Year studies		
		1st day of 1st Month	Last day of 6th Month	Last day of 12th Month	Last day of 18th Month	Last day of 24th Month
A	**Physiochemical Parameters**					
1	Color	Brown colored Granules	Brown colored Granules	Brown colored Granules	Brown colored Granules	Brown colored Granules
2	Odor	Characteristic	Characteristic	Characteristic	Characteristic	Characteristic
3	Taste	Bitter & Salty	Bitter & Salty	Bitter & Salty	Bitter & Salty	Bitter & Salty
4	Particle size	Pass Through 12 no mesh	Pass Through 12 no mesh	Pass Through 12 no mesh	Pass Through 12 no mesh	Pass Through 12 no mesh
5	Loss on Drying	4.91%	5.12%	5.65%	5.85%	5.96%
6	pH (10% Aq Solution)	4.05	4.02	4.43	4.45	4.55
7	Total Ash Content	2.80%	2.85%	3.12%	3.35%	3.56%
8	Water Soluble Extractive Values	53%	51%	49%	49%	47%
9	Alcohol Soluble Extractive Value	18%	16%	14%	13%	13%
10	Acid Insoluble ash value	0.68%	0.68%	0.67%	0.67%	0.67%
11	Water Soluble ash Value	1.36%	1.35%	1.37%	1.38%	1.40%
B	**Bitter residue**	3.72%	3.64%	3.29%	3.20%	3.15%
C	**Total Tannins**	26%	25%	25.55%	25.60%	24%
D	**Total Saponin**	3.1%	2.8%	2.8%	2.7%	3.4%
E	**Total Bacterial Count**	$50x10^3$	$26x10^4$	$35x10^5$	$25x10^4$	$40x10^5$
F	**Total Yeast & Mould**	$24x10^1$	$40x10^2$	$75x10^3$	$45x10^2$	$65x10^3$
G	**Specific Pathogen**					
	Staphylococcus aureus	Absent	Absent	Absent	Absent	Absent
	Escherichia coli	Absent	Absent	Absent	Absent	Absent
	Pseudomonas aeruginosa	Absent	Absent	Absent	Absent	Absent
	Salmonella Species	Absent	Absent	Absent	Absent	Absent

DISCUSSION

Stability studies ensures that the specified efficacy and quality of active compounds in product, will be the same in time period, under specified storage conditions considered as shelf life or expiration of the product, which maintains its identity, strength, quality and purity. Globally stability studies on herbal formulation are not having a same standardized procedure as found in case of modern medicines. In India medicines used in Ayurveda therapy includes the ingredients with herbal origin is a common scenario. It is very challenging to maintain shelf life of these products with herbal origin but central council for Research in Ayurvedic sciences recommends the guidelines on this[15]. In this study all the suggested parameters were followed and 24 months shelf life has been calculated.

CONCLUSION

This study support that the constac granules were successfully examines using real time stability study and found as safe up to 24 months under recommended conditions. Which ensures efficacy and quality of active compounds in this formulation.

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