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Optimization formulation and evaluation of senna tablets for the treatment of constipation

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Abstract

In the recent year more people throughout the world are turning to use of medicinal product in healthcare system. Herbal drugs technology is implemented for converting botanical materials into medicine and universal trend has been shifted from synthetic to herbal medicine i.e. return to nature. Hence, an attempt is made to develop tablet formulation of Senna using standardized extract of senna and volatile oils of ajowan. Senna extract granules were prepared by wet granulation method and ajowan oil was encapsulated using β -cyclodextrin before compression. Different excipients are used during the optimization of the tablet formulation. All the parameters are within the range for tablets. The result revealed that we have successfully optimized formulation and evaluation of tablet formulation of Senna as per the official monograph on I.P.

Keywords: Senna, ajowan, β -cyclodextrin, healthcare system etc.

Introduction

Herbal drugs have been used since ancient times as medicines for the treatment of wide range of disease ailment. As per World Health Organization (WHO) herbal drugs are classified into three groups: raw plant material, processed plant materials and herbal medicinal products. An increase in popularity of herb based formulation has attracted attention of various modern pharmaceutical streams. As a result formulators have started implementing advanced techniques to make traditional dosage forms into more consumer friendly & scientifically proven preparations. For example, essential oil (carminatives) once consumed with sugar or jaggary are now available in soft gelatin capsules form. Ultimately commercialization has bring the need to ensure quality and uniformity of medicament in particular dosage form made at a manufacturing unit by implementation of advanced technologies in the field of pharmaceutical science. It is possible to produce herbal medicines in the line with modern medicines. Senna is an effective and long established remedy for constipation because it contains a powerful natural laxative called anthraquinone and is approved by the World Health Organization (WHO).

Senna is used as a laxative for the management of constipation & for the evacuation of the bowel earlier to the diagnostic tests of the gastrointestinal and colorectal region. Thymol is the main active constituent of ajowan that shows antispasmodic, stimulant, tonic and carminative properties. The overdose of senna causes griping and cramp which is removed by the optimum dose of ajowan oil. Senna is the most common stimulant laxatives used as active ingredient. This ingredient has been choice of researchers; therefore, ample scientific data is available on the same. Senna is official in various pharmacopoeias and also covered by World Health Organization in its monograph as medicinal plants. Sennosides are the active chemical constituents of senna which is used for the relief of constipation. Sennosides have been reported to induce griping. Due to the side effect use of senna has reduced recently. There is a need to address this issue by formulators. Use of carminatives can reduce griping. Carminatives such as mint, cloves, fennel, cumin and ajowan have been reported to have antispasmodic activity. Among these carminative ajowan has much valued for antispasmodic action, Therefore, a combination of senna and ajowan in the form of tablet to provide the benefit of sennosides without griping.

Material and Methods

The Senna extract was gifted by natural remedies, Bangalore, Karnataka, Ajowan oil is taken from Rama Pharmaceutical. Other excipients such as Microcrystalline cellulose (MCC) (PH 101), Microcrystalline cellulose (MCC) (PH 102) (Rama Pharmaceuticals), Pre-gelatinised

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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.

Preformulation Parameters

Steps involved in Granulation Techniques

Encapsulation of Ajowan Oil

Various experiments were done with different excipients to encapsulate ajowan oil into a suitable matrix system.

Experiment 1: Adsorption Method

The weighed quantity of Syloid and starch was taken in planetary mixer and mix uniformly and then ajowan oil was adsorbed on these excipients. Separately the PEG 6000 was taken in beaker and melt at 50-60 °C and then oil adsorbed powder was mixed in decreasing order of temperature in PEG 6000 and keep it in refrigerator for 30 minute and then pass it from 20 # sieve to obtain uniform granules.

Observation: The granules formed by this trial batch were not having good flow properties and having stickiness hence this material was not suitable for compression.

Experiment 2: Adsorption Method

The granules of Silicone dioxide (Syloid) are prepared by using Starch Paste (10%) and HPMC (10%).

Granulation by Starch Paste: The weighed quantity of Syloid was taken in planetary mixer and slowly starch paste (10%) was added to the Syloid and mix properly and then wet mass was passed through 20 # sieve. Then uniform size granules obtained was dry in vacuum tray dryer and used for the adsorption of ajowan oil.

Granulation by HPMC: The weighed quantity of Syloid was taken in planetary mixer and slowly starch paste (10%) was added to the Syloid and mix properly and then wet mass was passed through 20 # sieve. Then uniform size granules obtained was dry in vacuum tray dryer and used for the adsorption of ajowan oil.

Observation: The granulation prepared by method A (Starch) were not enough hard to use for compression and also granules prepared by method B (HPMC) were hard but adsorption of ajowan oil was not enough to be use them from further for tablet compression.

Experiment 3: Adsorption Method

A combination of starch: MCC (PH-101): Syloid was taken in ratio 1:1:1 and granule were prepared with 10% starch paste further the adsorption of ajowan oil was carried out.

Observation: The adsorption of Ajowan oil was not enough.

Experiment 4: Adsorption Method

Make the granules of following excipients in the mention proportion liquid glucose (60 gm): Maltodextrin (20gm): MCC (30gm)

Procedure: Warm the liquid glucose at 55-60 °C in a beaker

and add Maltodextrin and mix properly and then add MCC and dry this paste in vacuum spray drier and pass these dry granules in Sieve no 16 # sieve to obtain granules.

Observation: It was observed that granules were formed are very hard and light but the oil encapsulation efficiency was very low.

Experiment 5: Adsorption Method

Prosolv SMCC was taken and dried at 60 °C and granules were prepared by using liquid glucose and these granules were passed through 20 # sieve and dry these granules in vacuum tray dryer and oil was adsorbed on these granules.

Observation: Encapsulation efficiency was very low.

Experiment 6: Spray Drying Method

An Emulsion was prepared using:

Maltodextrin	18 g
Gum Arabic	42 g
Water	200 ml
Ajowan Oil	3.7 ml

Procedure: The 200ml Milli-q-water was taken in the stainless steel tank with mechanical stirrer and gum Arabic was dissolved properly. Separately oil was adsorbed in maltodextrin and then mixed in gum Arabic solution using high speed of mechanical stirrer. This emulsion was used in spray dryer to make microcapsule of ajowan oil.

Observation: In spray drying method the microcapsules of ajowan oil were prepared and it was observed that losses during the process are very high.

Experiment 7: Adsorption Method

Procedure: Weigh quantity of maltodextrin was taken in planetary mixer and ajowan oil was mixed uniformly with maltodextrin. And then PVP was added and mix properly to make granules followed by addition of calcium carbonate to make free flow of granules.

Observation: During tablet compression proper hardness was not obtained and the rate of evaporation of essential oil was very high during accelerated stability conditions.

Experiment 8: Molecular Inclusion method

Material: β -cyclodextrin

Procedure: Weight quantity of β -cyclodextrin taken in planetary mixer and ajowan oil was mixed uniformly with β -cyclodextrin. And then PVP was added and mix properly to make granule followed by addition of calcium carbonate to make free flow of granules.

Observation: The encapsulation efficiency of β -cyclodextrin was high, stable, and hard having good flow property to the microcapsule of the ajowan oil during tablet compression and stability testing conditions. This trail was found suitable and further optimized to get a standard test procedure for obtaining the microcapsule of ajowan oil.

Physical Characteristics of Granules

Parameters	RCS ₁	RCS ₂	RCS ₃	RCSA ₁	RCSA ₂	RCSA ₃	RCSA ₄
Moisture Content (% w/w)	3.62	3.84	4.25	4.17	3.90	3.93	3.65
Angle of Repose (θ)	27.69	28.36	28.46	27.35	21.12	22.32	22.17
Carr Index (%)	20.62	18.16	17.30	11.76	12.49	12.18	12.16
Hausner Ratio	1.12	1.13	1.13	1.09	1.08	1.14	1.29

Formulation of Senna Tablets
Trial batches of Senna tablet

Trial Batch Excipients (mg)	RCS ₁	RCS ₂	RCS ₃	RCSA ₁	RCSA ₂	RCSA ₃	RCSA ₄
Senna Extract	150	150	150	150	150	150	150
Ajowan oil	----	----	----	36	36	36	36
β-cyclodextrin	----	----	----	----	64	64	64
Microcrystalline cellulose (PH101)	175	325	337	136	163	161	159
Croscarmellose sodium	35	35	35	35	35	35	35
Microcrystalline cellulose (PH 102)	----	----	----	----	10	12	14
PVP	----	----	----	40	40	40	40
Calcium carbonate	----	----	----	20	20	20	20
Pre-gelatinised starch	60	60	60	60	60	60	60
Magnesium Stearate	9	9	9	9	9	9	9
Talc	9	9	9	9	9	9	9
Aerosil	----	----	----	4	4	4	4
Maltodextrin	----	----	----	101	----	----	----
Dibasic calcium phosphate	150	----	----	----	----	----	----
Syloid	12	12	----	----	----	----	----
Average wt of tablet (mg)	600	600	600	600	600	600	600

Methodology of Formulation of Tablet

Granulation of Senna Extract: First, the active botanical ingredient Senna and Microcrystalline cellulose (PH 101& 102) as a diluents & Pre-gelatinised starch as binder were taken and uniformly mixed together in a planetary mixer. The Milli-q-water was added slowly added to the powder blend and kneaded well. The speed of the planetary mixer was increased. The resulted wet mass was dried in hot air oven to a moisture content of 4-6%.

Sizing of Granules: The resulting dried granules were passed through 20 # sieve.

Encapsulation of Ajowan oil: First the β-cyclodextrin was taken in planetary mixer and the weight quantity of ajowan oil was added and mixes till the ajowan oil completely encapsulated in β-cyclodextrin. After that PVP was added and mixed properly with ajowan β-cyclodextrin complexes to make uniform granules. Finally the calcium carbonate was added to the Ajowan oil granules to give free flow to the granules.

Sizing: The resulting dried granules were passed through 20 # sieve.

Mixing and Lubrication: The mix both active ingredient and add Croscarmellose sodium, Talc, Magnesium stearate and Aerosil (200).

Compression: Tablets were produced on a tablet compression machine using caplet tooling.

Optimized Formula of Senna Tablet

S. No.	Ingredients	Unit formula quantity/mg
1	Senna Extract	150
2	Ajowan Oil	36
3	β-cyclodextrin	64
4	Microcrystalline cellulose (PH101)	159
5	Microcrystalline cellulose (PH102)	14
6	Pre-gelatinised starch	60
7	Croscarmellose sodium	35
8	Polyvinylpyrrolidone (PVP)	40
9	Calcium carbonate	20
10	Talc	9
11	Magnesium Stearate	9
12	Aerosil (200)	4

Physical Characteristics of Optimized Tablet

Parameters	RCS ₁	RCS ₂	RCS ₃	RCSA ₁	RCSA ₂	RCSA ₃	RCSA ₄
Moisture content(% w/w)	3.63	3.87	4.38	4.26	3.98	4.12	3.67
Thickness (mm)	5.14	5.13	5.10	5.12	5.16	5.11	5.12
Hardness(Kg/cm ²)	6.1	6.4	5.6	5	5.2	6.7	8
Friability(% w/w)	0.1278	0.1214	0.1953	0.9319	0.9218	0.0846	0.0724
Disintegration Time (Minutes)	37 Min	39 Min.	36 Min.	31 Min.	29 Min.	27 Min.	26 Min.

Result and Discussion

Tablets of Senna extract and ajowan oil was successfully formulated. Preformulation studies of the extract of Senna and ajowan oil have shown that the extract and essential oil used

in the development of tablets formulation were of good quality. Moisture pick up study carried out on the extract revealed that extract of Senna was highly hygroscopic in nature and all the further processes are required to be carried

out in dehumidified air conditioned area maintained at temperature less than 25 °C and relative humidity less than 50%. A physical compatibility study of extract and essential oil with possible excipients was performed and no physical incompatibility was observed except with Syloid. In spray drying method the microcapsules of ajowan oil were prepared and it was observed that losses during the process are very high. At the same time loss of volatile oil due to high drying temperature was noticed.

Maltodextrin was also tried for the adsorption of essential oil and it was observed that rate of evaporation of essential oil was very high and during compression hardness could not be achieved. For the encapsulation of essential oil various techniques were tried like adsorption, spray drying and molecular inclusion complexes mechanisms using various excipients like Maltodextrin, PEG 6000, MCC (PH102), β -cyclodextrin. β -cyclodextrin as the encapsulating material was best excipients for this purpose in comparison to other with respect to properties of the tablet.

Senna extract granules were prepared by wet granulation method and ajowan oil was encapsulated using β -cyclodextrin before compression. The result revealed that the batch RCSA⁴ fulfill all the criteria as per the official monograph on tablets (I.P.).

Conclusion

There are various preparations in the market containing essential oil in the form of liquid preparation, capsule or powders formulation. Tablet dosage form having essential oil is an ingredient was achieved during this research. This was possible only by encapsulating the essential oil into matrix of β -cyclodextrin. Though a number of other methods like adsorption, spray drying was tried only encapsulated oil was possible to run on tablet compression machine. No physical and chemical degradation was observed during three months stability studies. 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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