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Possible use of *Ocimum basillicum* Linn. seed mucilage as release retardant

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Abstract

Various hydrophilic polymers such as methylcellulose, PEGs, HPMC are used in formulation of sustain release preparations but the high cost of synthetic polymers and environmental pollution by chemical industry has made the scientist in developing country to enter into an era where plant products serves as alternative to synthetic products because of local accessibility, environmentally friendly nature, lower prices and non toxic compared to imported synthetic products. Today we have number of pharmaceutical excipients from natural world such as guar gum, tragacanth, xanthan gum which are used to formulate oral sustained release formulations. The present study was undertaken to study the natural polymer and explore its use as a release retardant. Various methods for extraction of polymer were developed and the yield by the microwave assisted extraction was found to be 31.46%. The polymer was evaluated for various parameters as per Indian Pharmacopoeia. The loss on drying, ash value, solubility, swelling index were well within the official limits. The release retardant property of separated mucilage was determined successfully by using polymer and calcium phosphate dibasic in 3:1 proportion using 2 % HPMC in 70 % alcohol as binder..

Keywords: Natural polymer, Microwave assisted extraction, Calcium phosphate dibasic.

INTRODUCTION

In recent years, water-swellable polymers have attracted considerable attention in the field of drug delivery systems. The swellable, hydrophilic polymers such as polyvinylalcohol, hydroxyl propyl cellulose, methylcellulose and hydroxyl propyl methylcellulose (HPMC) are quite popular in designing of controlled drug delivery dosage forms with HPMC being the most widely used among all.[10] However, these semi-synthetic polymers are relatively expensive the scientist in developing country are entering into an era, in which plant products serves as alternative to synthetic products because of local accessibility, environmentally friendly nature, lower prices and non toxic compared to imported synthetic products. Herbs are non-polluting renewable resources for sustainable supplies of cheaper pharmaceutical products. Number of plant-based pharmaceutical excipients are available and researchers have explored the utility of these plant-based materials as pharmaceutical excipients. Majority of investigations on natural polymers in drug delivery systems are centered on polysaccharides and proteins, due to their ability to produce a wide range of materials and properties based on their molecular structures

The present study was undertaken to separate mucilage from the seeds of *Ocimum Basilicum* Linn. and explore its use as a release retardant. The seeds of *Ocimum basilicum* Linn, also known as Tulsi in Marathi are available as very small black coloured seeds containing high proportion of mucilage. It is official in IP, BP and USP. It is used in food and pharmaceuticals at a dose level of 5-7 g, twice-a-day. [1] *Ocimum basilicum* Linn. has the ability to swell 10-12 times of its original volume and form a hydrogel.[2] It could serve as natural immobilized source of agriculturally based polysaccharides. It is biocompatible, Inexpensive, chemically inert, non-absorbable, environment friendly and easily available.

Various methods for extraction of polymer from the seeds were developed and the yield by the microwave assisted extraction was found to be highest i.e. 31.46%. The polymer was evaluated for various parameters as per Indian Pharmacopoeia. The loss on drying, ash value, solubility, swelling index were well within the official limits. The release retardant property of separated mucilage was determined successfully by using polymer and calcium phosphate dibasic in proportion of 3:1 ratio using 2 % HPMC in 70 % alcohol as binder.

MATERIALS AND METHODS

Oscimum seeds were purchased from local market HPMC was procured from Thermosil Fine Chem Industries, Bhosari, Pune. Calcium phosphate dibasic, Magnesium stearate was obtained by the Sahyadri Scientific Suppliers, Islampur, Pune.

Isolation of mucilage

The seeds of *Ocimum basilicum* Linn. contain the mucilage around the outer layer. The major problem in isolation of mucilage is that it swells but does not separate from the seeds. Because of this, general methods for the separation of mucilage are not applicable to separate the seed mucilage and hence, different procedures were tried to separate the seed mucilage.

A. In first method, the seeds (10 g) were boiled with distilled water (100 ml) for 15 min and the mass was filtered through Buchner funnel without filter paper. The retained residues were boiled with distilled water (50 ml) for 15 min and the combined liquid was passed through eight folds of muslin cloth. The mucilage was precipitated from the filtrate by adding ethanol. The precipitated mucilage was dried in an oven at 45 º C till it was completely dried. The powder was weighed to calculate the yield.

B. In this method, the seeds (10 g) were soaked for 12 h in distilled water (100 ml) and then added to a blender to separate mucilage from seeds. After blending for 15 min the mass was passed through eight folds of muslin cloth. The mucilage was precipitated from the filtrate by adding 100 ml of acetone. The powder was weighed to calculate the yield after drying at 45 º C for 6 h.

C. In this method, the seeds (10 g) were soaked for 12 h in distilled water (100 ml) and crushed in blender for 15 min. The dispersion was boiled for 30 min and the mass was passed through eight folds of muslin cloth. The mucilage was precipitated from the filtrate by adding acetone. The powder was weighed to calculate the yield after drying at 45 º C for 6 h.

D. In this fourth method, the seeds (10 gm) were powered for 5 min in mechanical blender and soaked in distilled water (300 ml) for 24 hr in a round bottom flask. It was boiled for 1 hr under reflux with occasional stirring kept aside for 2 hr for the release of mucilage into water. The material was filtered through an eight fold muslin cloth and hot distilled water (50ml) was added through the side of the marc and squeezed well in order to remove the mucilage completely. Equal volume of ethanol was added to the filtrate to precipitate the mucilage and kept inside a refrigerator for one day for effective settling. It was filtered and dried completely in an oven at 45^0C, powered and weighed to calculate the yield.

E. In this last method, the seeds (10 gm) were powered in a mechanical blender for 5 min and soaked in distilled water (300 ml) for 24 hr in 1000 ml beaker. It was kept in microwave oven along with a glass tube inside to prevent bumping. It was subjected to microwave irradiation at 180 W intensity for 40 min. the beaker was removed from the oven and kept aside for 2 hr for the release of mucilage into water. Then the material was filtered through the eight fold muslin cloth and hot distilled water (50 ml) was added through the side of marc and squeezed well, equal volume of ethanol was added to the filtrate to precipitate the mucilage and kept inside the refrigerator for effective settling of mucilage. It was filtered and dried at 45^0C in an oven. The mucilage was powdered and weighed to calculate the yield. [13, 14, 15]

Physicochemical characterization of polymer:

The separated mucilage was evaluated for solubility, swelling index, loss on drying, ash value, density and compressibility index and angle of repose. The evaluation was carried out as per the procedures described below and the results obtained are shown in, [Table 1]

1. **Solubility** is expressed in terms of "parts" representing the number of milliliters (ml) of the solvent in which 1 g of the solid is soluble. Solubility of the powder was determined in different solvents at 20 º as per IP 96.

2. **Swelling characteristics** of the separated mucilage powder was studied in different media such as 0.1 N hydrochloric acid, pH 7.4 phosphate buffer and distilled water. One gram of powder was moistened with 0.5 ml ethanol (95%) and volume was made up to 10 ml with respective medium. The cylinder was shaken vigorously every 10 min for 1 h and allowed to stand for 3 h. The volume occupied by mucilage powder was measured. The test was carried out in triplicate and the average value of swelling index was recorded as shown in [Table 1].

3. As the inherent moisture may influence the stability of the tablet dosage form containing moisture sensitive drugs, moisture content of the separated mucilage was detected by **loss on drying** method. The sample (1 g) was heated at 105 º until constant weight in a hot air oven and percentage loss of moisture on drying was calculated using the formula,

LOD (%) = (weight of water in sample / weight of dry sample) × 100

4. The **total ash** was determined by placing 3 g of the ground air-dried material in a crucible, spreading the material in an even layer and igniting it by gradually increasing the temperature to 550 º C until it is white, indicating the absence of carbon. The crucible was cooled in a desiccator, weighed and the content of total ash in mg per g of air-dried material was calculated.

a. Acid-insoluble ash is the residue obtained after boiling the total ash with dilute hydrochloric acid and igniting the remaining insoluble matter. To the crucible containing the total ash, 25 ml of hydrochloride acid TS was added, covered with a watch glass and boiled gently for 5 min. The watch glass was rinsed with 5 ml of hot water this liquid was added to the crucible. The insoluble matter on an ash less filter paper was collected and washed with hot water until the filtrate is neutral. The filter paper containing the insoluble matter was transferred to the original crucible, dried on a hot plate and ignited to constant weight. The residue was allowed to cool in a desiccator for 30 min, weighed without delay and the content of acid insoluble ash in mg per g of air-dried material was calculated.

b. For water soluble ash instead of 25 ml hydrochloride acid, 25 ml water was added and the remaining procedure was same as that for the acid insoluble ash value.

5. The **specific gravity** was determined by using the 0.15% w/v solution of polymer.

6. The polymer was also tested for the **pH** by using 1% w/v solution of polymer.

Preparation of granules using separated mucilage

Granules containing **polymer** and **calcium phosphate dibasic** in 3 : 1 proportion were developed by conventional wet granulation technique using 2 % **HPMC** in 70 % alcohol as a binder. The wet mass was passed through 20 mesh and the resulting granules were dried at 50° for 3 h in a hot air oven. The dried granules were sized through 40 mesh size and lubricated with **magnesium stearate** and **aerocil** mixture.

Evaluation parameters for prepared granules

Bulk density was measured by taking accurately weighed powder into a graduated cylinder of tapped density apparatus and the volume was measured and recorded as bulk volume.

The cylinder was tapped until powder bed volume reached a constant value (100 taps) and the volume was recorded as tapped volume. The bulk density, tapped density and compressibility index were calculated using the equations,

bulk density= mass/bulk volume;
tapped density= mass/tapped volume and
compressibility index= [tapped density-bulk density] /tapped density

The angle of repose is used to characterize a flow property of powder material. It was determined by fixed height funnel method.
The results for the evaluation of granules prepared are given in [Table 2]

Preparation of tablets using separated mucilage

The uniformly mixed blend was compressed into 100 mg tablets using flat face round tooling on a rotary tablet machine. The tablets were stored in tightly closed glass container and evaluated for following parameters in triplicate.

Evaluation of tablets

1. Uniformity of diameter and thickness

To determine uniformity of the diameter and thickness 20 tablets were selected and diameter as well as thickness was measured using vernier caliper. The average diameter and thickness of the tablet was determined. The test requirements were met if non-of the individual diameter and thickness value deviated by ±5% of the average.

2. Hardness

A simple device, Monsanto Hardness tester was used to check the hardness of the tablet. A tablet was placed vertically between the jaws of the tester. The two jaws placed under tension by a spring and screw gauge. By turning the screw, the load was increased, and at collapse the applied pressure from the spring was measured in kg. The test was done on six tablets.

3. Friability

In this test, tablets were subjected to Roche Friability tester. The tablets (6 tablets) were dedusted and weighed. The tablets were then tumbled in the tester by rotating the drum 100 times. The tablets were weighed again and percent friability was calculated by the following formula.

$$F\% = (W_o - W) / W_o \times 100$$

Where,

F = friability
W_o = initial weight of the six tablets
W = final weight of the six tablets.

Tablets that loose less than 0.5 to 1% of weight are generally considered acceptable. The experiment was done in triplicate.

7. Swelling index determination:

The tablets were placed in a basket made of stainless steel mesh. The tablet with the basket was accurately weighed before being vertically placed in a beaker containing 30ml of aqueous medium having different pH values of 2, 4, 6, 8 and distilled water. At prefixed intervals, excess fluid was removed and the set containing the swollen tablet was weighed. The weight of the swollen tablet was calculated. The swelling index (S.I.) was determined from the following relation:

$$S.I. = (W_t - W_0) / W_0$$

Where,

W_t is the weight of the swollen tablet at each time interval *t*,
W_0 is the initial weight of the tablet.
The experiment was carried out in triplicate.

8. Radial and axial swelling study:

The initial diameter and thickness of the tablets were measured and the tablets were then kept in distilled water (30ml). The increase in height and diameter was measured at pre-selected time intervals up to eight hours. To evaluate the swelling, the equilibrium degree of swelling *(Q)* was calculated from radial and axial swelling ratio;

$$Q = V_t/V_o = (R_t/R_o)^2 \times I_t/I_o$$

where,

V_t and V_o are volumes,
R_t and R_o are radii and
I_t and I_o are thickness at time t and time zero, respectively.

The experiment was carried out in triplicate.
Results for the evaluation for tablet are shown in [Table 3]

RESULTS AND DISCUSSION

1. Isolation and Evaluation of Mucilage

Five different laboratory developed methods were tried for the separation of seed mucilage. The yield was 8%, 10%, 14%, 23.10% and 36.19% w/w for method A, method B, method C, method D and method E respectively. The mucilage obtained by each method was a light brown powder. The mucilage powder that was obtained by method E was evaluated further because of highest yield.

The powder was slightly soluble in water and practically insoluble in organic solvents. Swelling characteristics studies revealed that the swelling was affected by pH of the medium and powder showed good swelling ratio in distilled water. The loss on drying, ash value were well within official limits, shown in [Table 1]

Table 1: Physicochemical Evaluation of isolated mucilage

Parameters	Results
Solubility	Soluble in cold water and hot water, forming viscous colloidal solution.
Swelling index	11%
Ph	6-7
Specific gravity (g/ml of 0.15%w/v solution)	1.1 gm/ml
Loss on Drying	11.8 %
Total ash	7.72
Acid insoluble ash	0.57 %
Water soluble ash	6.532 %

2. Evaluation of Granules prepared using Seed Mucilage

Wet granulation method was chosen to formulate the release retardant tablets.

Wet granulation is the process in which a liquid is added to powder in a vessel equipped with any type of agitation that will produce agglomerates or granules. Granulation by dry compaction has many limitations. It does not lend itself to all tablet formulations because it depends on the bonding properties of dry powder added as carrier to the drug there by increasing the size of the tablet. In wet granulation, the bonding properties of the liquid binders available are usually sufficient to produce bonding with minimum additives. The granules prepared were evaluated for Bulk density, Tapped density, Compressibility index, Angle of repose and Flow rate and the results obtained are shown in [Table 2]

Table 2: Evaluation of granules prepared

Parameters	Results
Weight of granules	2.7gm
Bulk density(gm/cm^2)	0.40
Tapped density	0.48
Compressibility index	16%
Angle of repose	$18^0$77'
Flow rate	2.7gm/sec

3. Evaluation of Tablets

The tablets were prepared by using the prepared granules and studied for their hardness, percent friability, diameter, thickness and swelling capacity. From these study the hardness was found to be 1 kg/cm^2 , percent friability was 0.14 %, average diameter and average thickness were 0.7 cm and 0.9 cm respectively. At maximum the tablets were found to swell up to the average diameter 1.41 cm and the average thickness up to 1.30 cm, between the time period of 120 to 210 min i.e. it maintain this property for minimum 2 hrs. from the total time period of 7.5 hrs. [Table 3]

Table 3: Evaluation of tablets prepared using polymer as release retardant

Properties	Results
Hardness	1 kg/cm^2
Percent friability	0.14%
Average diameter	1.41 cm
Average thickness	1.305 cm
Swelling capacity	Radial

4. Swelling Behaviour of Tablet Formulation

Since the present study was on the swellable matrix, diffusion controlled drug delivery system; swelling behavior of the tablet formulation was studied by determining swelling index and radial and axial swelling pattern.

Tablets swelled more radially than axially as evident from the data of normalized diameter and thickness [Table 4]

Table 4: Radial and axial swelling of tablets in distilled water

Time (min)	Normalized Diameter(mm)	Normalised Thickness(mm)
0	0.7	1
15	1.5	1.0
30	1.5	1.5
60	1.6	1.7
90	1.7	1.7
120	1.8	1.8
180	1.7	1.7
240	1.7	1.6
300	1.5	1.5
360	1.0	1.0
420	0.6	0.0
480	0.0	

Normalized diameter = diameter at time t / diameter at time zero
Normalized thickness = thickness at time t / thickness at time zero

After 2 h insignificant increase in equilibrium degree of swelling Q was noticed. The probable slower swelling in terminal phase may be due to decreased diffusion of water into the matrix. Tablets swelled more radially than axially. Swelling rate reached steady value after two hours.

CONCLUSION

From the present study, it was concluded that the mucilage separated from *Oscimum basilicum* Linn. could be used as release retardant in the tablet formulations as it shows very good swelling capacity and maintain this property for minimum 2 hrs. The material showed good gelling property during isolation but after its isolation this property was lost. If the gelling property is retained by any other separation method, it may be studied as a gelling agent as well as matrixing agent in sustained release tablets.

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