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Research Article

ISOLATION OF MUCILAGE FROM CYDONIA VULGARIS PERS. SEEDS; AND ITS EVALUATION AS A TABLET BINDER

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ABSTRACT

Gums and mucilages are preferably used as they are natural materials, for formulating conventional and novel dosage formulations. Natural materials have advantages over synthetic ones since they are chemically inert, nontoxic, less expensive, bio degradable and available in sufficient quantities. The study elaborates isolation of mucilage from the seeds of Cydonia vulgaris Pers. and explores it as tablet binder. The mucilage was evaluated for all the parameters viz. solubility, swelling index, loss on drying, total ash, acid insoluble ash, microbial load and pH as per official monographs. The results confirmed that evaluation parameters were well within the limits. The binding efficiency of isolated mucilage was equivalent to Acacia. The prepared batches were evaluated for hardness, friability, weight variation, % drug content and in vitro dispersion time. The results of isolated mucilage from Cydonia vulgaris Pers. seeds were very promising.

Keywords: Seed mucilage, Cydonia vulgaris Pers., Binder, Natural excipient.

INTRODUCTION

Binders are pharmaceutical excipients that are commonly employed in tablet formulations to impact cohesion on powder mix and hence improve on the flow properties of the granules.[1] Binders act by causing aggregation of powders thereby forming granules through the process of granulation. They modify the cohesive properties of the granules by promoting the formation of strong cohesive bonds between such particles.[2] There are growing concerns for the safety on pharmaceutical excipients derived from animal sources.[3] Plant gums and exudates are getting screened for their use as pharmaceutical adjuvants. Mucilages are used for their binding, thickening, stabilizing and humidifying properties in medicine.[4] Newer uses in cosmetics and textiles had hiked up demand [5] and screening of gums had become a vital pharmaceutical interest.[6]

Mucilage is most commonly used as adjuvant in the manufacturing of different pharmaceutical dosage forms. They possess a variety of pharmaceutical properties, which include binding [7], disintegrating [8], suspending [9], emulsifying [10], and sustaining properties [11], at different proportion in different pharmaceutical dosage forms. Natural mucilages are preferred over semi-synthetic and synthetic materials due to their non-toxic, low cost, free availability, emollient and non-irritating nature[12].

Cydonia vulgaris Pers. is the cultivated and economically important species of genus Cydonia. Cydonia vulgaris Pers. (Cydonia oblonga Miller) is a small shrub belonging to the family Rosaceae and is a native to Southwest Europe and Minor Asia. The Cydonia vulgaris is commonly medicinally used as demulcent, in treatment of asthma. Other usages of the plant are as a source of flavor in marmalade, liqueur, candies, brandy, jelly and preserves. [13] The seeds of Cydonia vulgaris Pers seeds,, also known as Quince seeds in English and Beedana in Gujarati contain a high proportion of mucilage. The present study deals with the isolation of the mucilage from the seeds of Cydonia vulgaris Pers. and its application as binding agent in tablet formulation.

MATERIALS AND METHODS

Materials

Cydonia vulgaris Pers. seeds were procured form LVG, Ahmedabad. Lactose and Paracetamol were kindly gifted by Montage laboratory, Himatnagar. All other materials used were of pharmaceutical grade. Instruments used were single punch tablet machine (Cadmach machines Ltd., Ahmedabad), weighing balance- Shimadzu AX 2000 (Shimadzu Corporation, Japan), hot air oven (Sun air instrument Ltd., Ahmedabad), Monsanto hardness tester (Shital scientific industry, Mumbai), friabilator- Model EF2 (Electrolab Mumbai) disintegration apparatus- Model ED2 (Electrolab, Mumbai) and dissolution apparatus- Model TDT-06T (Electrolab, Mumbai).

Isolation of mucilage

Cydonia vulgaris Pers. seed mucilage (CVM) was extracted and purified as per method described.[12] Plant material was dried in sunlight and/or in oven (105°C) to retain its properties unchanged. Plant material was treated with petroleum ether to remove pigments and fats. Then the material was dried at room temperature. The material was soaked in water for 5 h, boiled for 30 min and allowed to stand for 30 min so that mucilage was released in water. The material was squeezed from eight muslin bag to remove the marc. Equal volume of acetone was added to filtrate to precipitate mucilage. The mucilage was separated, dried in a temperature less than 50°C and powder was sieved through 20 # sieve and stored in dessicator.

Phytochemical screening of mucilage

The phytochemical properties such as presence of carbohydrate, protein, flavanoids, sterols, alkaloids, tannins, saponins, resin, phenol, and terpenoids were determined as per standard tests. [13]

Physicochemical characterization of mucilage

Solubility test

The isolated mucilage was evaluated for solubility in water, acetone, chloroform and ethanol in accordance with the British pharmacopoeia specifications. [15]

Swelling index

Swelling index was measured according to procedure mentioned in British Pharmacopoeia, 2004. [15] Swelling characteristics of the separated mucilage powder was studied in distilled water. 1.0 g of powder was moistened with 0.5 ml ethanol (95%) and volume was made up to 25 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 and the value of swelling index was recorded.

Loss on drying

The method adopted was that specified in the B.P 2004 for acacia. [15] 1.0 g of the sample was transferred into each of several Petri dishes and then dried in an oven at 105°C until a constant weight was obtained. The moisture content was then determined as the ratio of weight of moisture loss to weight of sample expressed as a percentage.

Total ash and acid insoluble ash determination

Ash content was estimated by the measurement of the residue left after combustion in a furnace at 450°C. The ash obtained from the

determination of the ash was boiled with 25 ml of 2M hydrochloric acid solution for 5 min and the insoluble matter was filtered and washed with hot water and ignited and the subsequent weight was determined. The percent acid insoluble ash was calculated. [15]

Microbial Load

Microbial count for separated mucilage powder was performed as outlined in IP 96 for total aerobic microbial count using plate count method. [16]

pH determination

This was done by shaking a 1% w/v dispersion of the sample in water for 5 min and the pH determined using a pH meter (MK VI, India). [17]

Micromeritic properties of mucilage

The angle of repose of mucilage was determined by the fixed funnel method.[18] The loose bulk density (LBD) and tapped bulk densities (TBD) were determined by using a density apparatus (Lyser Instruments, Ahmedabad, India). The Carr's index (%) and the Hausner ratio were calculated. [19]

FTIR study

The FTIR spectrum of Cydonia vulgaris Pers. Mucilage was carried out.

Elemental Analysis

Elemental analysis of carbon, hydrogen and nitrogen in mucilage was carried using a Perkin Elmer, series II-2400 determinator.

Preparation of granules

All the materials were passed through a 100 mesh sieve before use. The tablets were prepared by wet granulation method. The compositions of tablets were given in table 1. Paracetamol, starch and lactose were thoroughly mixed and the solution of the mucilage of specified concentration was prepared by dispersing the mucilage in water. The mucilage solutions were used for moistening the powder mixture, for preparing tablets to evaluate the binding potential. The wet mass was then passed through sieve no. 10 and dried at temperature not exceeding 50°C in a hot air oven for 30 minute. The dried granules were rescreened through a sieve no 20. Acacia gum was used as standard binder.

Table 1: Composition of different batches of Paracetamol tablet using mucilage as a binder.

Ingredients	F1 (2%)	F2 (4%)	F3 (6%)	S1 (6%)
Paracetamol (mg)	100	100	100	100
Lactose	155	149	143	143
Starch	30	30	30	30
Acacia	-	-	-	18
Mucilage	6	12	18	-
Talc	6	6	6	6
Magnesium stearate	3	3	3	3
Total weight (mg)	300	300	300	300

Preparation of tablets

The granules were lubricated with Magnesium stearate (1%) and talc (2%) and further mixed. The resultant blends were tableted to 300 mg using a single punch tablet press (single station tablet compression machine, Cadmach, Ahmedabad, India).

Evaluations of the Granules and Tablets

Micromeritic properties of granules

Prior to compression of tablets, granules were evaluated for its characteristic parameters. Angle of repose was determined by fixed funnel method. [18] Bulk density and Tapped densities were determined by using a density apparatus (Lyser Instruments, Ahmedabad, India). The Carr's index (%) and the Hausner ratio were calculated. [20]

Characteristics of tablet

Prepared tablets were evaluated for the different physicochemical parameters such as hardness, friability, weight variation, drug content and tablet thickness. Briefly, hardness was determined by using Monsanto hardness tester. Friability was determined using Roche friability testing apparatus. Weight variation, disintegration test and drug content were performed according to the IP procedures. [16] Tablet thickness was measured using Vernier calipers.

In vitro Drug Release Studies

In vitro dissolution of Paracetamol fast disintegrating tablets was studied in USP XXIII type-II dissolution apparatus (Electrolab, Model-TDT 06N) employing a paddle stirrer at 50 rpm using 900 ml of 0.1N Hydrochloric acid at 37±0.5ºC as dissolution medium. Aliquots of dissolution medium (5 ml) were withdrawn at specified intervals of time and analyzed for drug content by measuring the absorbance at 257 nm. The volume withdrawn at each time interval was replaced with fresh quantity of dissolution medium. Cumulative percent of Paracetamol released was calculated and plotted against time. [16]

RESULTS AND DISCUSSION

Phytochemical Properties of mucilage

Cydonia vulgaris Pers. Mucilage (CVM) was extracted, purified and subjected to phytochemical screening. Table 2 shows Prelimininary phytochemical screening of Cydonia vulgaris Pers. The phytochemical screening showed positive test for carbohydrate, which confirmed purity of mucilage.

Table 2: Prelimininary phytochemical screening of Cydonia vulgaris Pers. Mucilage

Active constituents	Cydonia vulgaris Pers. mucilage
Carbohydrate	+
Protein	-
Flavanoids	-
Tannins	-
Saponins	-
Sterols	-
Alkaloids	-
Triterpenes	-
Glycosides	-
Fats & oils	-
Resins	-
Phenols	-
Diterpenes	-

Physicochemical Properties of mucilage

Isolated mucilage was subjected to various physicochemical parameters such as solubility, swelling index, loss on drying, total ash, acid insoluble ash as shown in table 3. The mucilage extracted from the seeds of Cydonia vulgaris Pers. is slightly soluble in water and a dispersion of it yielded a off white, slimy solution. The mucilage was practically insoluble in methanol, acetone and chloroform. Tragacanth which was used as a reference sample gave a similar solubility profile.

The swelling characteristic of CVM was studied in distilled water. The swelling in water was found to be 23. Generally, the results show that CVM has high swelling index suggesting that the mucilage may perform well as binder/disintegrant/matrixing agent. [21]

The moisture content of CVM was low, suggesting its suitability in formulations containing moisture sensitive drugs. Given suitable temperature moisture will lead to the activation of enzymes and the proliferation of micro organisms, thereby affecting the shelf life of most routine formulations. It is important to investigate the moisture content of a material because the economic importance of an excipient for industrial application lies not only on the cheap and ready availability of the biomaterial but the optimization of production processes such as drying, packaging and storage. [22]

The total ash and acid insoluble ash value of CVM was found to be 3.5 and 0.5% w/w respectively. Ash values reflect the level of adulteration or handling of the drug. Adulteration by sand or earth is immediately detected, as the total ash is normally composed of inorganic mixtures of carbonates, phosphates, silicates and silica. Therefore, the low values of total ash and acid insoluble ash obtained in this study indicate low levels of contamination during

gathering and handling of crude Cydonia vulgaris Pers. [15]

The microbial load for bacteria and fungi of CVM was measured and found to be within official limit. The data are shown in Table 3.

A 1% w/v suspension of CVM in water gave a pH of 5.6 while that of tragacanth was 5.3. Knowledge of the pH of an excipient is an important parameter in determining its suitability in formulations since the stability and physiological activity of most preparations depends on pH. [21]

Table 3: Results of physicochemical characteristic

Parameters		Cydonia vulgaris Pers.	Tragacanth
Solubility		Slightly soluble in water, practically insoluble in acetone, methanol and chloroform.	Slightly soluble in water, practically insoluble in acetone, methanol and chloroform.
Swelling index	In distilled water	23	18
Loss on drying		8%	4%
Total ash		3.5%	4%
Acid insoluble ash		0.5%	1.5%
Microbial Load	Bacteria (CFU/g)		
	Fungi (CFU/g)		
pH		5.60	5.30

Micromeritic Properties of Mucilage

The bulk and tapped densities give an insight on the packing and arrangement of the particles and the compaction profile of a material. [23] The compressibility index and angle of repose of CVM was 7.2% and 28.65° respectively, implying that the CVM has a good flow with moderate compressibility, unlike tragacanth with a very poor compressibility index of 1.30% and an angle of repose 20.31° shown in table 4. This is important in scale up processes involving this material as an excipient in a pharmaceutical formulation. Modification of formulations containing this mucilage for the improvement of flow properties during process development will therefore be minimal compared to tragacanth (e.g., inclusion of glidants or agents to aid in feeding). [20]

Table 4: Micromeritic properties of mucilage

Parameters		Cydonia vulgaris Pers.	Tragacanth
Density of powder	Bulk density (g/cc)	0.58	0.76
	Tapped density (g/cc)	0.625	0.77
Compressibility index		7.2 %	1.30 %
Hausner's ratio		1.07	1.01
Porosity		0.069	0.026
Angle of repose		28.65	20.31

FTIR study of Cydonia vulgaris Pers. Mucilage

The interpretation for FTIR study is shown in Fig 1. FTIR spectrum of Cydonia vulgaris Pers. Mucilage is reported in table 5.

Table 5: Interpretation of FTIR study of Cydonia vulgaris Pers. Mucilage

Frequency (cm^{-1})	Assignment
3409	N-H stretch of primary amine
2926.67	C-H stretch of aliphatic amine
1654	N-H bending of primary amine
1416	C-H bending
1381	C-H bending vibration of $-CH_2$
1044	C-N stretch of primary amine

Elemental Analysis

The quantitative elemental analysis is shown in Table 6. The results show the presence of Carbon, Hydrogen and Nitrogen. The low level of nitrogen is suggestive of amino acid (peptide) crosslink in the sample. The ratio of carbon to hydrogen is just over 6:1 indicating, long with a good number of unsaturation due to aromatic rings and/or polysaccharide composition.

Compatibility studies of Mucilage and model drug (Paracetamol)

Differential scanning calorimetry

The melting point of Paracetamol is reported to be 169-170.5˚C. The DSC thermogram of Paracetamol and mixture of Paracetamol and mucilage (CVM) are shown in Fig. 2. The thermograms of drug and mucilage of Cydonia vulgaris Pers. shows that there is no change in melting point which confirms that there exist no interaction.

FTIR studies

Further drug polymer interaction was checked by comparing the IR spectra of the physical mixture of drug with the Mucilage of Cydonia vulgaris Pers. used with the IR spectrum of pure drug. Frequencies of functional groups of pure drug remained intact in physical mixture containing Cydonia vulgaris Pers. (Fig 3), so it was concluded that there was no major interaction occurred between the drug and Cydonia vulgaris Pers. used in the study.

Micromeritic Properties of Granules

The results of micromeritic properties are presented in Table 7. For compression of materials, it is required to possess good flow and compacting properties. Values for angle of repose 20–30° generally indicate good flow property. A Hausner ratio of less than 1.25 and Carr's index of 12–16 indicate good flow.[19] The prepared formulation mixtures showed good flow properties as indicated by low values of angle of repose, Carr's index and Hausner ratio.

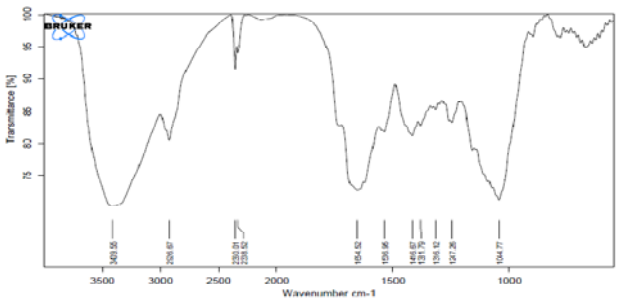

Fig. 1: FTIR spectrum of Cydonia vulgaris Pers. Mucilage.

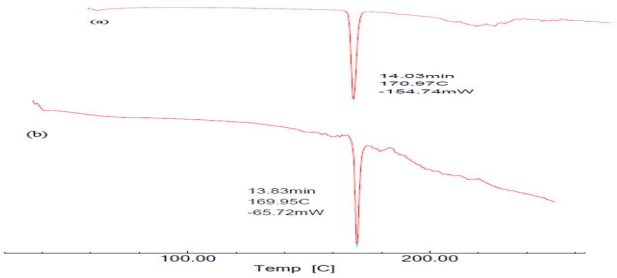

Fig. 2: (a) DSC of Paracetamol drug (b) DSC of CVM with Paracetamol drug

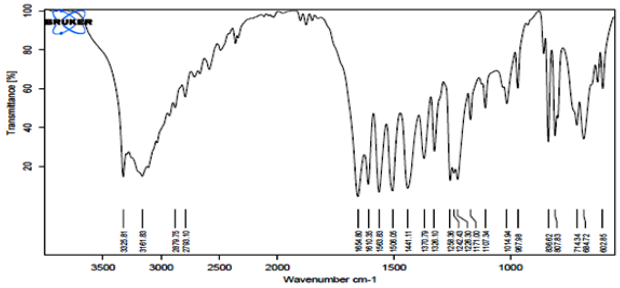

Fig. 3: FTIR spectrum of Cydonia vulgaris Pers. mucilage with drug Paracetamol

Properties of prepared Paracetamol tablet

The tablets of Paracetamol were prepared by wet granulation method employing Cydonia vulgaris Pers. mucilage, starch and lactose. Acacia (6%) was taken as a standard. A total of three formulations for mucilage, F1 (2%), F2 (4%), F3 (6%) and a formulation containing 6% acacia (C1) were designed (table 1). As the blends were free flowing (angle of repose <30º, and Carr's index <15%) tablets obtained were of uniform weight (due to uniform die fill), with acceptable variations as per IP specification i.e., below ±7.5%. Drug content was found to be in the range of 95 to 101%, which is within acceptable limits. Hardness of the tablets was found to be about 3-3.5 kg/cm^2. Friability below 1% was an indication of good mechanical resistance of the tablets. The data are shown in table 8.

In vitro drug release studies

In vitro dissolution studies on the formulations were carried out in 0.1 N Hydrochloric acid, and the various dissolution parameter values viz., percent drug dissolved in 1 hr, 2 hr, 3 hr, and 4 hr (D_1, D_2, D_3 and D4) are shown in Table 9 and the dissolution profiles depicted in fig 4. The results showed that the formulation F2 showed faster drug release than Formulation F1 and F3.

Table 6: Elemental composition of *Cydonia vulgaris* Pers. Mucilage

Sample name	%C	%H	%N
Cydonia vulgaris Pers. Mucilage	39.71	6.28	6.26

Table 7: Micromeritic properties of granules

Granule properties	F1	F2	F3	S1
Angle of repose (Θ)	± 0.21	± 0.43	± 0.79	29.12±0.15
Bulk density (g/cc)	0.27±0.005	0.33±0.006	0.41±0.009	0.25±0.01
Tapped density (g/cc)	0.31±0.009	0.41±0.002	0.50±0.001	0.29±0.02
Carr's Index	12.90±0.29	19.51±0.15	18.00±0.92	13.79±0.15
Housners' ratio	1.14±0.008	1.24 ±0.005	1.21±0.019	1.16±0.028
Granule strength (%)	7.12±0.08	6.51±0.06	5.78±0.02	5.19±0.80

Values are expressed as mean ±S.D. (n=3).

Table 8: Evaluation of tablets using CVM as a binder

Batch code	Average weight (mg)	Diameter (mm)	Thickness (mm)	Hardness (kg/cm²)	Friability (%)	Disintegration time (sec)	Drug content (%)
F1	312±1.25	9.12	3.15	6.2	0.85	172±1.33	98.48
F2	299±1.33	9.10	3.20	6.8	0.90	213±2.66	99.26
F3	302±1.25	9.11	3.16	6.4	0.82	242±2.33	98.63
S1	304±1.04	9.10	3.12	4.78	0.92	326±1.03	98.23

Values are expressed as mean ±S.D. (n=3).

Table 9: In vitro drug release studies

Time (hr)	Cumulative % drug release			
	F1	F2	F3	S1
0	0	0	0	0
1	28.56	32.15	31.12	30.56
2	44.92	51.19	46.25	48.12
3	52.35	62.35	66.32	58.69
4	69.98	77.69	72.12	71.82

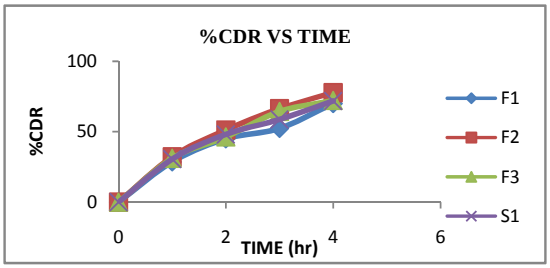

Fig. 4: In vitro cumulative drug release versus time profile

CONCLUSION

As per pharmacopoeia, disintegration time of uncoated tablets should be <15 min. it was found that the tablets using 2-6% concentration of isolated C. vulgaris Pers. mucilage exhibited disintegration time and hardness within the standard limit. All formulations showed >75% cumulative percentage drug release within 4 hours. The formulations exhibited a better and more consistent release as compared to standard formulation using acacia as a binder. Taking all the above parameters into consideration, the study has revealed a good potential of C. vulgaris Pers. mucilage as a binder for tablet formulations.

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