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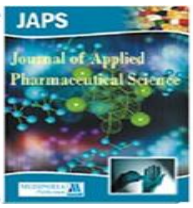

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Isolation of Mucilage from *Cydonia vulgaris* Pers. Seeds and its Evaluation as Superdisintegrant

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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 disintegrant. 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 disintegrating efficiency of isolated mucilage was equivalent to cross-povidone . The prepared batches were evaluated for hardness, friability, % drug content, wetting time, water absorption ratio and *in vitro* dispersion time. The results of isolated mucilage from *Cydonia vulgaris* Pers. were very promising.

Key words: Seed mucilage, *Cydonia vulgaris* Pers., Fast disintegrating tablets, Natural excipient.

INTRODUCTION

Excipients are additives, used to convert active pharmaceutical ingredients into pharmaceutical dosage form suitable for administration to patients (Patel et al., 2007). New and improved excipients continue to be developed for conventional drug delivery systems and also to meet the needs of modern and better formulations. Mucilages are most commonly used as adjuvants in the manufacturing of different pharmaceutical dosage forms. They possess variety of pharmaceutical properties, which include binding (Kulkarni et al., 2002), disintegrating (Patel et al., 2007), suspending (Mithal and Kasid, 1965), emulsifying (Mithal and Kasid, 1964), and altering release properties (Kulkarni et al, 1997) at different proportion in different pharmaceutical dosage forms. Natural mucilages are preferred to semi-synthetic and synthetic materials because of their low cost, free availability, emolliency, non-irritating nature and non toxicity (Jani et al., 2009).

Cydonia vulgaris Pers. (*Cydonia oblonga* Miller) is a small shrub belonging to the family Rosaceae and is native to Southwest Europe and some parts of Asia. *Cydonia vulgaris* is medicinally used as demulcent and in the treatment of asthma. Other usages of the plant are as a source of flavor in marmalade, liqueur, candies, brandy, jelly and as preservatives (Kirtikar and Basu, 1999). The seeds of *Cydonia vulgaris* Pers. is also known as *Quince seeds* in English and *Beedana* in Gujarati. It contain a high amount of mucilage. The present work aims to isolate mucilage from *Cydonia vulgaris* Pers. seeds and explore it as disintegrant in tablets.

MATERIALS AND METHODS

Materials

Cydonia vulgaris Pers. seeds were procured form a local vendor. Avicel pH-102 (MCC) and Paracetamol were gifted by Montage laboratory, Himatnagar. All other materials used were of pharmaceutical grade.

Isolation of mucilage

Cydonia vulgaris Pers. seed mucilage (CVM) was extracted and purified as follows Plant material was dried in sunlight and/or in oven (105°C) to retain its properties. It was then treated with petroleum ether to remove pigments and fats and again dried. The material so obtained was soaked in water for 5 h, boiled for 30 min and allowed to stand for 30 min for the mucilage to be released as hydroextract. The material was also pressed through a muslin cloth and to marc was separated. Equal amount of acetone was added for precipitating mucilage. The mucilage, thus, separated was dried at a temperature less than 50°C and powder was passed through 20 # sieve and stored in a dessicator (Jani et al., 2009).

Phytochemical Screening of mucilage

The phytochemical properties for the presence of carbohydrate, protein, flavanoids, sterols, alkaloids, tannins, saponins, resin, phenol, and terpenoids were determined as per standard tests (Kokate, 2006).

Physicochemical characterization of mucilage

Solubility test

The isolated mucilage was evaluated for solubility in water, acetone, chloroform and ethanol in accordance with the official monograph specifications (British Pharmacopoeia, 2004).

Swelling index

Swelling index was measured in distilled water (British Pharmacopoeia, 2004).

Loss on drying

The method adopted was the same as that specified in the B.P 2004 for acacia (British Pharmacopoeia, 2004).

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 (British Pharmacopoeia, 2004). The ash obtained from the determination 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 (British Pharmacopoeia, 2004).

Microbial Load

Microbial count for separated mucilage powder was performed for total aerobic microbial count using plate count method (Indian Pharmacopoeia, 2007).

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 (Ohwoavworhua and Adelakun, 2005).

Micromeritic properties of mucilage

The Angle of repose (Liebermann et al., 1990), loose bulk density (LBD) and tapped bulk densities (TBD) were determined. The Carr's index (%) and the Hausner ratio were calculated (Wells and Aulton, 2007).

Elemental Analysis

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

Preparation of Paracetamol tablets using isolated mucilage

Table 1 depicts the composition of different batches. The resultant blends were tableted to 300 mg using a single punch tablet press.

Table 1: Composition of different batches of tablets of Paracetamol

Ingredients	F1	F2	F3	F4	F5
Paracetamol	100	100	100	100	100
Mucilage	-	6	12	18	-
Cross povidone	-	-	-	-	12
MCC	201	185	179	173	179
Magnesium stearate	3	3	3	3	3
Talc	6	6	6	6	6
Total(mg/tablet)	300	300	300	300	300

Evaluation of Paracetamol tablets

Micromeritic properties of Powder blend

Prior to compression of tablets, powder blend was evaluated for its characteristic parameters. Angle of repose was determined by fixed funnel method (Liebermann et al., 1990). Bulk density and Tapped densities were determined by using a density apparatus. The Carr's index (%) and the Hausner ratio were calculated (Emeje et al., 2006).

Characterization of tablets

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 (Indian Pharmacopoeia, 2007). Tablet thickness was measured using Vernier calipers.

Wettability studies and Water absorption test

The wettability studies were done according to the method described by Gohel et al., 1997. A glass petri dish was partially

filled with water and a tablet was placed on the surface of a band of filter paper supported on a glass slide. The uptake of water occurred from the lower surface of the tablet. The time required for water to reach the center of the upper surface of the tablet was noted as wetting time (Gohel et al., 1997). The wetted tablet was then weighed. Water absorption ratio 'R' was calculated using the equation

$$R - 100 \times \frac{W_a - W_b}{W_a}$$

Where w_a is weight of tablet after water absorption and w_b is weight of tablet before water absorption.

In vitro Drug Release Studies

In vitro dissolution was studied in USP XXIII type-II dissolution apparatus and measuring the absorbance at 257 nm. Cumulative percent of Paracetamol released was calculated and plotted against time (Indian Pharmacopoeia, 2007).

RESULTS AND DISCUSSION

Phytochemical Properties of mucilage

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	-

+ Present, - Absent.

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 off white, slimy solution. The mucilage was practically insoluble in methanol, acetone and chloroform. The swelling index in water was found to be 23 which suggests that the mucilage may perform well as binder/disintegrant/matrixing agent (Nasipuri et al., 1996).

The moisture content of CVM was low, suggesting its suitability in formulations containing moisture sensitive drugs and may lead to the activation of enzymes and the proliferation of micro organisms (Emeje et al., 2008). The total ash and acid insoluble ash value of CVM was found to be 3.5 and 0.5% w/w respectively which indicates low levels of contamination. (British Pharmacopoeia, 2004). The microbial load for bacteria and fungi of CVM was measured and found to be within official limit. The pH is 5.6 (Table 3).

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)	8	62
	Fungi (CFU/g)	1	9
pH		5.60	5.30

Micromeritic Properties of Mucilage

Table 4 reflects all the micromeritic properties of CVM and the results suggest it as an ideal tablet excipient (Emeje et al., 2009).

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

Elemental Analysis

The quantitative elemental analysis is shown in Table 5. The results show the presence of Carbon, Hydrogen and Nitrogen. The low level of nitrogen is suggestive of amino acid (peptide). The ratio of carbon to hydrogen is just over 6:1 indicating a long

chain. It may due to aromatic rings and/or polysaccharide composition.

Table 5: Elemental composition of *Cydonia vulgaris* Pers. Mucilage

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

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 Merck Index, 2001). The DSC thermogram of Paracetamol and mixture of Paracetamol and mucilage (CVM) are shown in Fig. 1. The thermograms of drug and mucilage of *Cydonia vulgaris* Pers. shows that there exists no interaction between drug and mucilage.

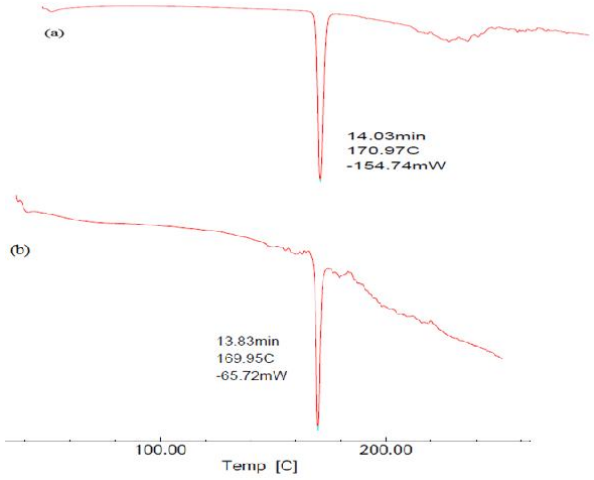

Fig 1: (a) DSC of Paracetamol drug (b) DSC of CVM with Paracetamol drug.

FTIR studies

Drug polymer non-interaction was confirmed by comparing the IR spectra of the physical mixture of drug and the Mucilage of *Cydonia vulgaris* Pers. with the IR spectrum of pure drug alone (Fig. 2).

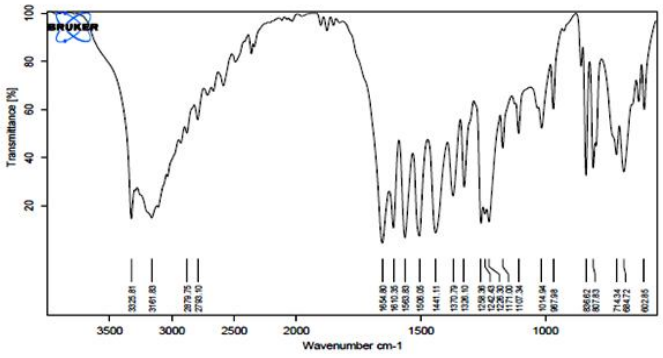

Fig 2: FTIR spectrum of *Cydonia vulgaris* Pers. Mucilage with drug Paracetamol.

Micromeritic Properties of Powder blend

The results of micromeritic properties are indicated in Table 6. The prepared formulation mixtures showed good flow properties as indicated by good values of angle of repose, Carr's index and Hausner ratio.

Table 6: Evaluation of powder blend

Formulation	Angle of repose (˚)	Carr's index (%)	Hausner ratio
F1	26.03 ± 0.28	14.12 ± 0.28	1.164 ± 0.004
F2	24.17 ± 0.37	14.02 ± 0.25	1.11 ± 0.006
F3	25.57 ± 0.81	15.33 ± 1.45	1.156 ± 0.020
F4	24.35 ± 0.52	14.12 ± 0.24	1.13 ± 0.002
F5	26.80 ± 1.87	16.51 ± 0.82	1.228 ± 0.012

Evaluation of prepared tablets

The tablets were prepared by direct compression method employing *Cydonia vulgaris* Pers. mucilage and crospovidone as super-disintegrants in different ratios along with microcrystalline cellulose. A total of five formulations, 1 standard (F5), 3 tests (F2-F4) and a control formulation F1 (without super disintegrant) 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/cm². Friability below 1% was an indication of good mechanical resistance of the tablets. Water absorption ratio and wetting time, which are important criteria for understanding the capacity of disintegrants to swell in presence of little amount of water were found to be in the range of 50-69% and 10-18 seconds, respectively (Table 7).

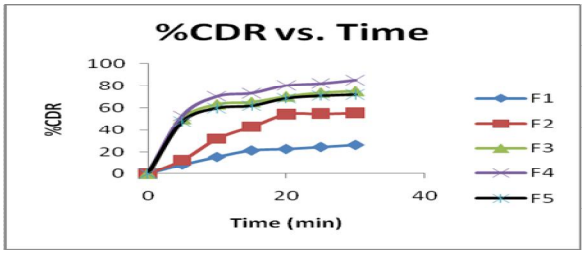

Fig 3: *In vitro* cumulative drug release versus time profile

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 5 min, 10 min, 15 min, 20 min, 25 min and 30 min (D_5, D_{10}, D_{15}, D_{20}, D_{25} and D_{30}), t_{50}%, t_{70}% and t_{90}% are shown in Table 8 and the dissolution profiles depicted in fig. 3. The results showed that the formulation F3 and F4 showed faster drug release than F5.

Table 7: Evaluation of prepared tablets

Parameters	F1	F2	F3	F4	F5
Hardness (kg/cm^2)	3.5	3	3	3.5	3.5
Thickness (mm)	2.6	2.7	2.6	2.6	2.7
Friability (%) ±SD	0.45	0.42	0.50	0.46	0.50
Disintegration time (sec) ±SD	244±0.86	18±1.3	11±0.66	10±0.33	23±0.46
Wetting time (sec) ±SD	230±1.83	55±1.25	36±1.06	18±1.12	49±0.92
Water absorption ratio (%) ±SD	50±0.62	59±0.12	63±0.23	69±0.36	61±0.58
% drug content ±SD	96.45±1.03	98.86±0.73	101.22±0.76	100.34±0.71	99.28±0.84

Table 8: *In vitro* dissolution data

Formulations	D_5	D_{10}	D_{15}	D_{20}	D_{25}	D_{30}	t_{50}	t_{70}	t_{90}
F1	8.23	15.46	21.36	22.65	24.39	26.28	>30	>30	>30
F2	12.56	32.19	43.33	54.78	55.12	55.88	17.98	>30	>30
F3	50.21	63.25	65.24	70.28	73.56	75.02	4.56	19.6	>30
F4	53.18	70.42	73.33	80.32	82.12	85.24	4.12	9.76	>30
F5	48.25	60.26	62.35	68.95	71.25	72.30	5.19	21.35	>30

CONCLUSION

From the present data, it can be concluded that the mucilage isolated from *Cydonia vulgaris* Pers. Could be used as a super-disintegrant in the tablet formulations as it shows very good disintegrating properties. During the process, the material showed good gelling property, which after isolation was lost. If the gelling property is retained by any other separation method. It may be exploited as a gelling agent. CVM may well be used as a binder due to its sticky nature when hydrolysed with water. The seed mucilage can also be used as a suspending agent.

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