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FORMULATION AND EVALUATION OF CIPROFLOXACIN DISPERSIBLE TABLETS USING *PLANTAGO OVATA* MUCILAGE IN COMPARISON WITH OTHER SUPERDISINTEGRANTS

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ABSTRACT

In the present work, an attempt has been made to study the superdisintegrant property of isolated mucilage powder of *Plantago ovata* by formulating the dispersible tablets of ciprofloxacin and comparing its efficiency with other super disintegrants like microcrystalline cellulose, crosspovidone and sodium starch glycollate. Drug compatibility with the mucilage was checked by FTIR studies and found to be intact and stable. The values of pre-compression and post-compression parameters evaluated were within the prescribed limits and showed good flow property. In all the formulations, friability was less than 1%, indicating that tablets had a good mechanical resistance. Drug content and weight variation for all the formulations were found to be within the acceptable limits. The formulations were also evaluated for wetting time, hardness, thickness, disintegration time, uniformity of dispersion, water absorption ratio and dissolution. The results of all the tests of the formulation prepared with *Plantago ovata* mucilage powder are similar to that of those formulations prepared using other superdisintegrants and the disintegration time was found to be 110 sec. The study also revealed that the isolated mucilage powder of *Plantago ovata* showed a better drug release of 99% over the other superdisintegrants, sufficing its applications as a superdisintegrant of natural origin.

Key words: Dispersible tablets, *Plantago ovata* mucilage, Synthetic super disintegrants.

INTRODUCTION

Tablet is the most popular dosage form among all existing today because of convenience of self administration, compactness and easy manufacturing. Convenience of

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administration and patient compliance are gaining importance in design of various dosage forms. This concept oriented research has resulted in bringing out many safer and newer drug delivery systems[1].

Dispersible tablets are intended to dissolve or disintegrate rapidly in the mouth for which various disintegrants either natural or synthetic are included in the formulation[2]. They are uncoated tablets that produce a uniform dispersion in water at room temperature without stirring. They are easier to swallow than capsules for pediatric, dysphasic patients, mentally ill, unco-operative and nauseated patients, those with conditions of motion sickness, sudden episodes of allergic attacks or coughing[3].

Mucilage is most commonly used as excipient in the manufacturing of various pharmaceutical dosage forms. Mucilages of natural origin are preferred over semi-synthetic and synthetic because of their non-toxic, low cost, free availability, emollient and non-irritating nature[4].

Mucilage of *Plantago ovata* seeds has various characteristics like binding, disintegrating and sustaining properties[5]. This is also used as suspending and thickening agent because of its high swelling factor and ability to form viscous solution[6].

Ciprofloxacin is a synthetic quinolone derivative. It is widely prescribed because of its safety, good tolerance and broad antibacterial spectrum[7].

EXPERIMENTAL

Materials and method

Ciprofloxacin was procured from Yarrow Chem Products, Mumbai. Isapghula seeds were purchased from local market. All others excipients used are of analytical grade.

Isolation of mucilage

The seeds were soaked in distilled water (20-30 times) for at least 48 hrs[8]. Then the seeds boiled for few minutes for complete release of mucilage into water. The material was filtered by squeezing in a muslin cloth to remove marc. Then equal volume of acetone was added to filtrate to precipitate the mucilage. The mucilage was separated and dried in an oven at a temperature less than 60ºC, powdered, sieved (# 80 mesh), weighed and stored in desiccator until further use[9].

Formulation of dispersible tablets

The dispersible tablets of ciprofloxacin were prepared by non-aqueous wet granulation method using absolute alcohol as the solvent. *Plantago ovata* mucilage powder, microcrystalline cellulose, sodium starch glycollate, crosspovidone were used as disintegrants, dicalcium phosphate as a diluent, PVP as a binder, aspartame as sweetener, purified talc as lubricant and aerosil as glidant (Table 1). The drug and other ingredients with half the quantity of disintegrant (intragranular disintegrant) were mixed together, sufficient quantity of alcohol was added and mixed to form a coherent mass. The wet mass was granulated using sieve No. 12 and the coarse granules formed were dried in a tray dryer (Tempo instruments and equipments, Mumbai) at 40^{o}C for 20 minutes and regranulated through sieve No. 18. The granules were further blended with the remaining quantity of the disintegrant (extragranular disintegrant), purified talc, aerosil and compressed into tablets using a 8 mm round concave punches in a rotary tablet machine 5 (Rimek, RSB-4 mini press Cadmach, Ahmedabad, India).

Table 1: Composition of different batches of ciprofloxacin tablets

Ingredients	F1 (mg)	F2 (mg)	F3 (mg)	F4 (mg)
Ciprofloxacin	100	100	100	100
Dicalcium phosphate	100	100	100	100
Isapghula mucilage powder	25	-	-	-
Microcrystalline cellulose	-	25	-	-
Crosspovidone	-	-	25	-
Sodium starch glycollate	-	-	-	25
Poly vinyl pyrrolidone	15	15	15	15
Purified talc	3	3	3	3
Aspartame	5	5	5	5
Aerosil	2	2	2	2

Drug-mucilage interaction studies

The physical mixture of pure drug sample and isolated mucilage powder in the ratio

1 : 1 were subjected to IR spectral studies using FTIR spectrophotometer (FTIR 8400 S, Shimadzu, Japan).

Evaluation of the tablets

Pre-compression parameters

The granules were studied for various micromeritic properties such as angle of repose, bulk density, tapped density, Carr's index and Hausner's ratio.

Post-compression parameters

Weight variation

Randomly twenty tablets were selected after compression and the mean weight was determined. The sample tablets were weighed individually and the deviation from the mean weight was calculated (USP XXVII).

Thickness variation

Ten tablets from each formulation were taken randomly and their thickness was measured with a micrometer screw gauge.

Hardness

The crushing strength of the tablets was measured using a Monsanto hardness tester. Six tablets from each formulation batch were tested randomly and the average reading noted.

Friability

Twenty tablets were weighed and placed in a Roche friabilator and rotated at 25 rpm for 4 min. The tablets were taken out, dusted and reweighed. The percentage friability of the tablets was calculated by the formula,

$$\text{Percentage friability} = \frac{\text{Initial weight - Final weight}}{\text{Initial weight}} \times 100$$

Drug content

Twenty tablets were weighed and powdered. An amount of the powder equivalent to 100 mg of ciprofloxacin was dissolved in 100 mL of 0.1 N HCl filtered, diluted suitably and estimated for the drug content at 277.5 nm using UV-Visible spectrophotometer (UV 160-Shimadzu, Japan).

Wetting time and water absorption ratio (R)[10]

Twice folded tissue paper was placed in a Petri dish having an internal diameter of 5 cm containing 6 mL of water. A tablet was carefully placed on the surface of the tissue paper in the Petri dish. The time required for water to reach the upper surface of the tablet and to completely wet it was noted as the wetting time.

Water absorption ratio (R) was then determined according to the following equation:

$$R = 100 \times (wa - wb)/wb$$

Where wb and wa were tablet weights before and after water absorption, respectively.

In-vitro disintegration time

In vitro disintegration time was measured by placing a tablet in 100 mL water maintained at 25°C. The time taken for the tablet to disintegrate completely was noted.

Uniformity of dispersion

Two tablets were placed in 100 mL of water and stirred gently until completely dispersed. A smooth dispersion was obtained which passed through a sieve screen with a nominal mesh aperture of 710 mm (sieve number 22).

In-vitro dissolution study

In-vitro drug release studies of all the formulations were carried out using multi basket tablet dissolution test apparatus (USP TDT 06 PL, Electrolab, Mumbai) at 50 rpm. 0.1 N HCl was used as the dissolution media with temperature maintained at 37 ± 1°C. Samples were withdrawn at different time intervals, diluted suitably and analyzed at 277.5 nm using Shimadzu UV-Visible spectrophotometer[7].

RESULTS AND DISCUSSION

The reported isolation method yielded 30% of mucilage powder from the seeds of *Plantago ovata*. Dispersible tablets each containing 100 mg of ciprofloxacin were prepared employing mucilage powder of *Plantago ovata*, microcrystalline cellulose, crosspovidone and sodium starch glycollate using non-aqueous wet granulation method (Table 1). The drug excipient interaction was studied by FTIR spectroscopy revealed that the drug was stable and intact in the mixture without any change in the principle peaks of the drug (Fig. 1).

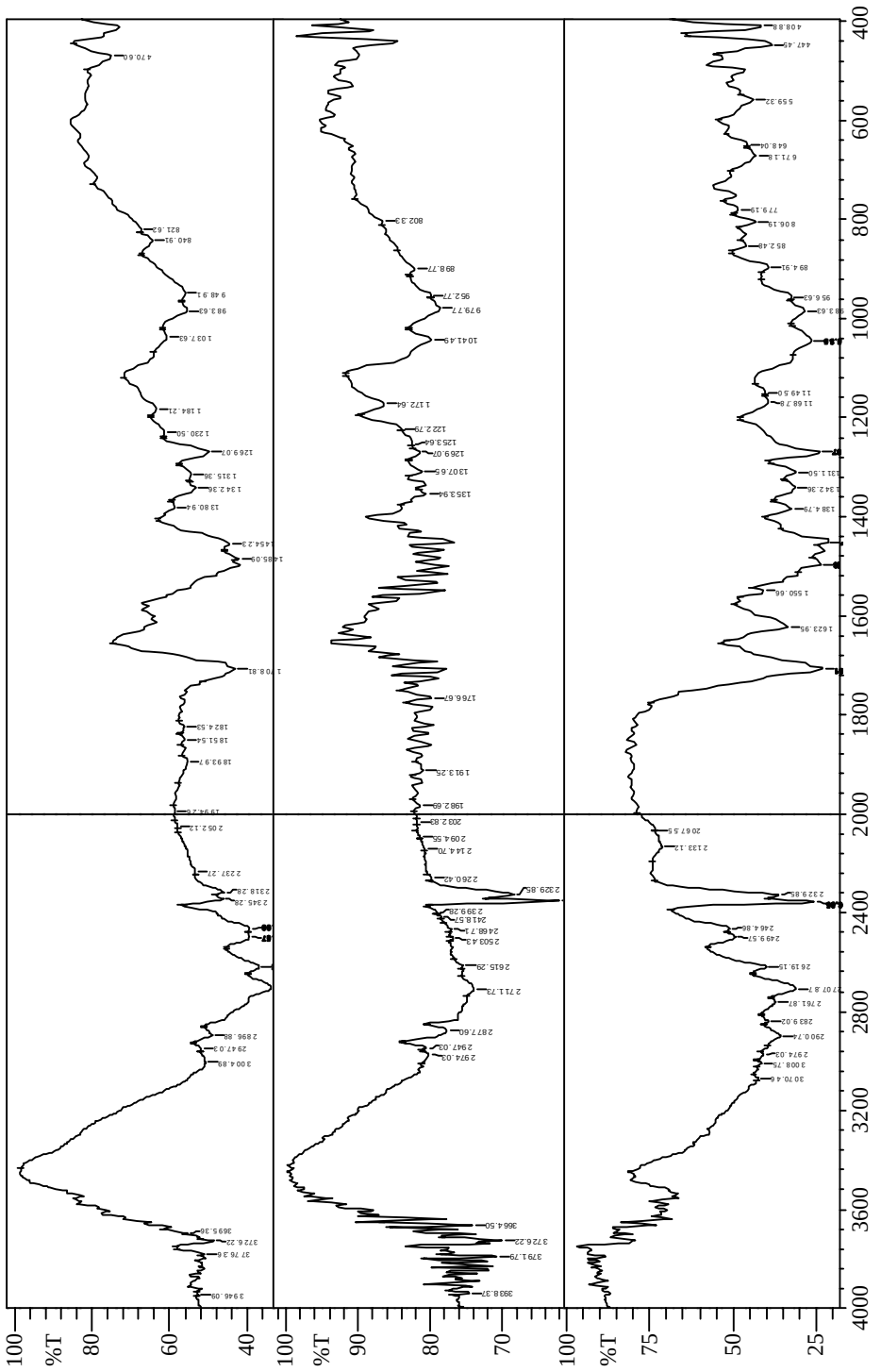

Fig. 1: FTIR spectra of drug, mucilage and the physical mixture

The values of pre-compression parameters evaluated were within prescribed limits and indicated good free flowing property as given in (Table 2).

Table 2: Pre-compression parameters of powder blend

Formulation code	Angle of repose (^{0})	Bulk density (gm/cc)	Tapped density (gm/cc)	Carr's index (%)	Hausner's ratio
F1	26.74	0.57	0.65	12.30	1.14
F2	25.96	0.575	0.65	12.30	1.130
F3	28.73	0.45	0.52	13.4	1.15
F4	27.29	0.535	0.605	11.5	1.130

The data obtained from post-compression parameters in all the formulations, friability was less than 1%, indicated that tablets had a good mechanical resistance. Drug content was found to be in the range of 97.88 to 100.2%, which is within acceptable limits. Hardness and thickness of the tablets were found to be in the range of 2.50-3.50 kg/cm^2 and 3.5-3.75 mm respectively. Water absorption ratio and wetting time of F1 was found to be 32% and 60 sec and for other formulations were found to be in the range of 26-52% and 59-87 sec respectively. The disintegration time for F1 was found to be 110 sec and for other formulations it is in the range of 49-290 sec (Table 3).

Table 3: Post-compression parameters of dispersible tablets of ciprofloxacin

Parameter	F1	F2	F3	F4
Weight variation (mg)	0.25 ± 0.01	0.257 ± 0.01	0.257 ± 0.01	0.25 ± 0.01
Thickness (mm)	3.75	3.70	3.64	3.56
Hardness (Kg/cm^2)	3.0	3.5	2.5	2.5
Friability (%)	0.49	0.4	0.38	0.77
Drug content (%)	97.88	99.9	100.2	99
In vitro disintegration time (sec)	110	290	49	180
Wetting time (sec)	60	87	59	67
Water absorption ratio (%)	32	52	36	26.9
Uniformity of dispersion	Passes	Passes	Passes	Passes

The drug release for F1 was found to be 99.8 % within 15 min and for other formulations it was released in 20 min except for F2 with 95 % drug release at 45 min (Table 4). It was very much clear that F1 exhibited better disintegration and dissolution behaviour suited for a dispersible tablet compared to other super disintegrants.

Table 4: *In vitro* release studies of different formulations

Formulation code	D_5 (%)	D_{10} (%)	D_{15} (%)	D_{20} (%)	D_{25} (%)	D_{30} (%)	D_{35} (%)	D_{40} (%)	D_{45} (%)
F1	55.49	83.60	99.8	-	-	-	-	-	-
F2	13.51	29.08	44.09	56.98	72.51	81.31	86.63	92.75	95.75
F3	71.99	89.86	93.29	97.84	-	-	-	-	-
F4	57.65	84.70	94.77	97.62	-	-	-	-	-

Where D_x (%) = % of drug released in respective min.

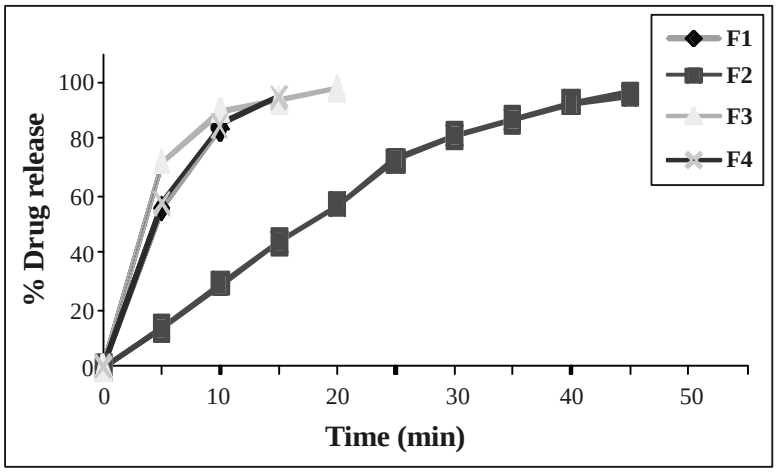

Fig. 2: Dissolution profile of all formulations

CONCLUSION

The isolated mucilage of *Plantago ovata* proved to be better super disintegrant for dispersible tablets in comparison with synthetic superdisintegrants. The mucilage evaluated for various physico-chemical parameters, showed the same characteristic similarities with the other established superdisintegrants. Hence *Plantago ovata* mucilage of natural origin could be successfully employed as superdisintegrant in the formulation of dispersible tablets.

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