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Development and Characterisation of Fast Disintegrating Tablet of Amlodipine besylate using Mucilage of Plantago ovata as a Natural Superdisintegrant

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Abstract: In present work an attempt has been made to prepare fast disintegrating tablets of Amlodipine Besylate by direct compression method using different concentrations of *plantago ovata* mucilage as a natural superdisintegrant. FT-IR studies revealed that there was no physico-chemical interaction between amlodipine besylate and other excipients. All formulation were evaluted for weight variation , hardness, friability, disintegration time ,drug content and dissolution. The formulations F5 shows less *in vitro* disintegration time 11.69sec with rapid *in vitro* dissolution within 16 mins. *In vitro* disintegration time decreases with increase in concentration of natural superdisintegrant. Therefore, we concluded that the dried isabgol mucilage as a superdisintergrant in the tablet is suitable for the formulation of fast disintegrating tablet.

Keywords: Amlodipine Besylate, Fast disintegrating tablets, *plantago ovata,* Superdisintegrant.

Introduction

The most popular solid dosage forms are being tablets and capsules, one important drawback of these dosage form for some patients, is the difficulty to swallow. Drinking water plays an important role in swallowing of oral dosage forms. For these reasons tablets that can fast dissolve or disintegrate in the oral cavity have attracted a great deal of attention. Fast disintegrating tablets (FDT) are solid single-unit dosage forms that are placed in the mouth, allowed to disperse/dissolve in the saliva and then swallowed without the need for water [1]. Fast disintegrating tablets are not only indicated for people who have swallowing difficulties, but also are ideal for active people. Fast disintegrating tablets are those when put on tongue disintegrates instantaneously releasing the drug, which dissolves or disperse in saliva[2,3].

Amlodipine besylate is a long-acting calcium channel blocker used in the treatment of chronic stable angina, vasospastic angina and hypertension[4]. Amlodipine is a sparingly soluble orally administered drug and the rate of absorption is often controlled by the rate of

dissolution. The rate of dissolution can be increased by incorporating the drug in a fast disintegrating dosage form[5].

Various natural substances gum karaya, modified starch and agar have been used in the formulations of fast disintegrating tablets. Mucilage of natural origin is preferred over semi-synthetic and synthetic substances because they are comparatively cheaper, abundantly available, non-irritating and non-toxic in nature. In the present investigation, the preparation and evaluation of fast disintegrating tablets by using different concentrations of natural superdisintegrant that is *plantago ovata* mucilage was studied. The reasons for selection of *plantago ovata* mucilage because it's high swelling index[6]. Mucilage of *plantago ovata* has various characteristics like binding, disintegrating and sustaining properties[7] .Hence, in present study, mucilage of *plantago ovata* was used to develop fast disintegrating tablets of Amlodipine Besylate. The concept of formulating fast disintegrating tablets (FDT) of Amlodipine Besylate using different concentrations of natural superdisintegrant which increase the water uptake with shortest wetting time and there by decrease the disintegration time of the tablets by simple and cost effective direct compression technique. The objective of present work was to develop fast disintegrating tablet Amlodipine Besylate by direct compression method and to study the effect of functionality differences of natural superdisintegrant *plantago ovata* mucilage on the tablet properties.

Materials and Methods

Amlodipine Besylate was obtained as a gift sample from Zydus Cadila Healthcare Ltd. Ahmedabad. *Plantago ovata* seeds were purchased from local market Amravati. Microcrystalline cellulose, Mannitol, talc and Magnesium stearate was procured from S.D Fine Chemicals, Mumbai, India and all other chemicals used were of analytical grade.

Isolation of Mucilage

Mucilage was isolated by soaking seeds of *plantago ovata* in water (20-30 times) for at least 48 hrs, boiled for 2 hrs subsequently mucilage was released into the water completely. With the help of the muslin cloth the mucilage was squeezed out and separated from seeds. The mucilage collected and precipitated using 3 times of 95% ethanol. Collected mucilage was dried in the oven at 50-55°. Dried mucilage was scraped and powdered using pestle and mortar. Powder was sieved using mesh no.60 [8].

Formulation of fast disintegrating tablets by direct compression method

Tablets were prepared according to the formula given in table 1. All the ingredients were passed through sieve 60 mesh separately. The drug & mannitol were mixed by taking small portion and further other ingredients were mixed in geometric order and tablets were compressed using 9 mm round flat punches to get tablets 150 mg weight. 50 tablets were prepared for each batch.[9-13]

Table 1: Composition of Amlodipine besylate tablet having weight 150 mg

Ingradients (mg)	Formulation Code				
	F1	F2	F3	F4	F5
Amlodipine Besylate	10	10	10	10	10
Plantago ovata mucilage	4.5	6	7.5	9	10.5
MCC (Avicel PH-102)	75	75	75	75	75
Mg stearate	1.5	1.5	1.5	1.5	1.5
Talc	2	2	2	2	2
Mannitol	57	55.5	54	52.5	51

Evaluation of fast disintegrating tablets

The prepared tablets were evaluated for weight variation, hardness, friability, *in vitro* disintegration time, wetting time, drug content, *in vitro* release study and FTIR studies.

Weight variation[14] **:** Twenty tablets were selected randomly from each formulation and weighed individually using a Ohaus digital balance. The individual weights were compared with the average weight for the weight variation.

Hardness and Friability[15] **:** Hardness of the tablets was measured using the Pfizer hardness tester. The friability of a sample of twenty tablets was measured using a USP type Roche friabilator. Pre-weighed tablets were placed in a plastic chambered friabilator attached to a motor revolving at a speed of 25 rpm for 4 min. The tablets were then dedusted, reweighed and percentage weight loss (friability) was calculated.

Drug content uniformity[16] **:** For the content uniformity test, ten tablets were weighed and pulverized to a fine powder, a quantity of powder equivalent to 10 mg of Amlodipine Besylate was extracted in 10 ml of methanol and liquid was filtered (0.22 µm membrane filter disc (Millipore Corporation). The drug content was determined by measuring the absorbance at 237 nm (using UV-VIS Spectrophotometer, Shimadzu 1800) after appropriate dilution with methanol. The drug content was determined using standard calibration curve. The mean percent drug content was calculated as an average of three determinations.

***In vitro* disintegration time**

The disintegration time for all formulations was carried out using tablet disintegration test apparatus. Six tablets were placed individually in each tube of disintegration test apparatus and discs were placed. The phosphate buffer pH 6.8 was maintained at a temperature of 37°±2°C and time taken for the entire tablet to disintegrate completely was noted.

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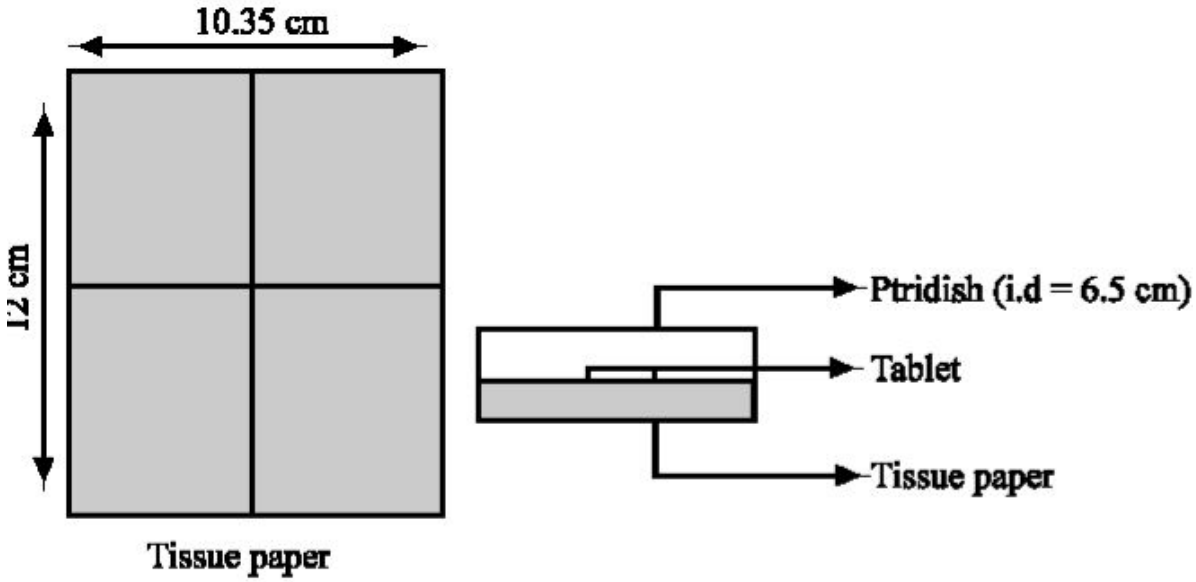
Wetting time and water absorption ratio (R)[17] **:** Twice folded tissue paper was placed in a Petri dish having an internal diameter of 6.5 cm to that added 6 ml of purified water. A tablet was carefully placed on the surface of the tissue paper in the Petri dish. The time required for water to reach 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:

$R=100 \times (w_a - w_b) / w_b$

Where; w_b and w_a were tablet weights before and after water absorption, respectively.



***In vitro* drug release study**[18-19]**:** *In-vitro* dissolution studies of the fast disintegrating tablets of Amlodipine Besylate formulation were performed according to USP XXIII Type-II dissolution apparatus (Electrolab, model TDT-06N) employing a paddle stirrer at 50 rpm using 900 ml of pH 7.2 phosphate buffer at 37 ± 0.5°C as dissolution medium. One tablet was used in each test. Aliquots of the dissolution medium (5 ml) were withdrawn at specific time intervals and replaced immediately with equal volume of fresh medium. The samples were filtered through 0.22 µm membrane filter disc and analyzed for drug content by measuring the absorbance at 237 nm. Drug concentration was calculated from the standard calibration curve and expressed as cumulative percent drug dissolved. The release studies were performed in triplicates.The average and standard deviation is calculated and showing in table 4.

FTIR Studies: The drug - excipients interaction were studied using FTIR. IR spectra for drug and powdered tablets were recorded in a Fourier transform infrared spectrophotometer with KBr pellets. The spectra were scanned over the 3600 to 400 cm-1 range.

Table 2: Pre-compression parameters of powder blend

Formulation Code	Bulk density	Tapped density	Angle of repose	Carr's index (%)	Hausner's Ratio
F1	0.517±0.02	0.612±0.01	31.25±0.74	15.52±1.23	1.184±0.02
F2	0.514±0.01	0.611±0.03	30.75±0.88	15.88±1.34	1.189±0.03
F3	0.524±0.02	0.621±0.02	32.12±1.24	15.62±1.26	1.185±0.03
F4	0.531±0.03	0.631±0.02	31.07±0.95	15.45±1.31	1.183±0.03
F5	0.519±0.02	0.619±0.01	33.14±0.98	16.16±1.24	1.193±0.02

Table 3: Post-compression parameters of fast disintegrating tablets

Formulations	Weight Variation	Hardness (kg/cm2)	Friability (%)	Wetting time(sec)	Water Absorption Ratio(%)
F1	Pass	3.0±0.19	0.66±0.24	13.73 ± 0.16	129.00 ± 0.59
F2	Pass	2.8±0.12	0.56±0.29	13.04 ± 0.23	135.24 ± 1.56
F3	Pass	2.6±0.11	0.52±0.21	12.84 ± 0.17	148.49 ± 0.84
F4	Pass	3.0±0.21	0.68±0.32	11.09 ± 0.56	156.12 ± 0.36
F5	Pass	2.8±0.17	0.54±0.24	8.12 ± 0.24	164.00± 0.75

Table 4: Evaluation of fast disintegrating tablets

Formulations	Disintegration time(sec)	Drug content(%)	Percentage drug dissolved After 16 minutes
F1	21.52± 0.67	99 ± 0.59	84.96 ± 0.69
F2	20.94 ± 0.51	99 ± 0.82	87.13 ± 0.36
F3	17.64 ± 0.24	98 ± 0.96	89.82 ± 0.49
F4	13.73 ± 0.62	99 ± 0.25	95.12± 0.52
F5	11.69 ± 0.69	101 ± 0.64	99.72 ± 0.14

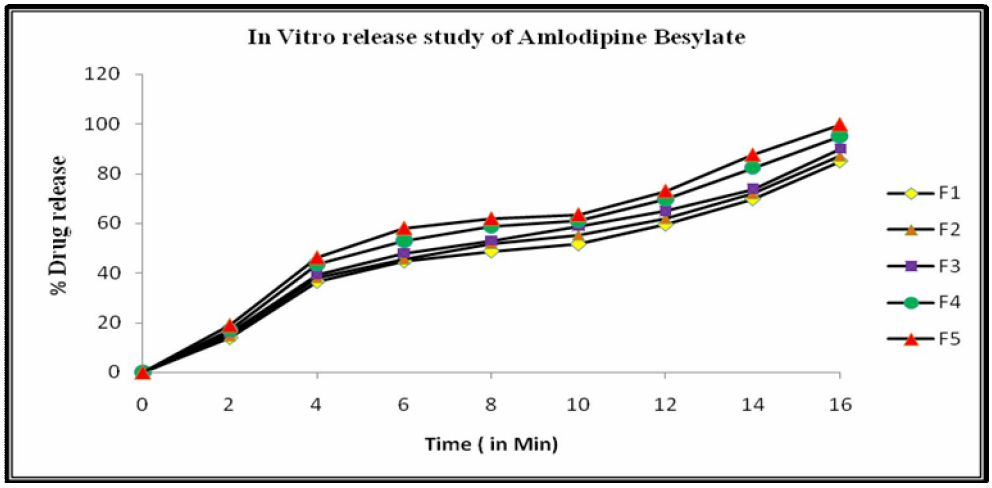


Fig. 1: Dissolution profiles of formulations F1 – F5

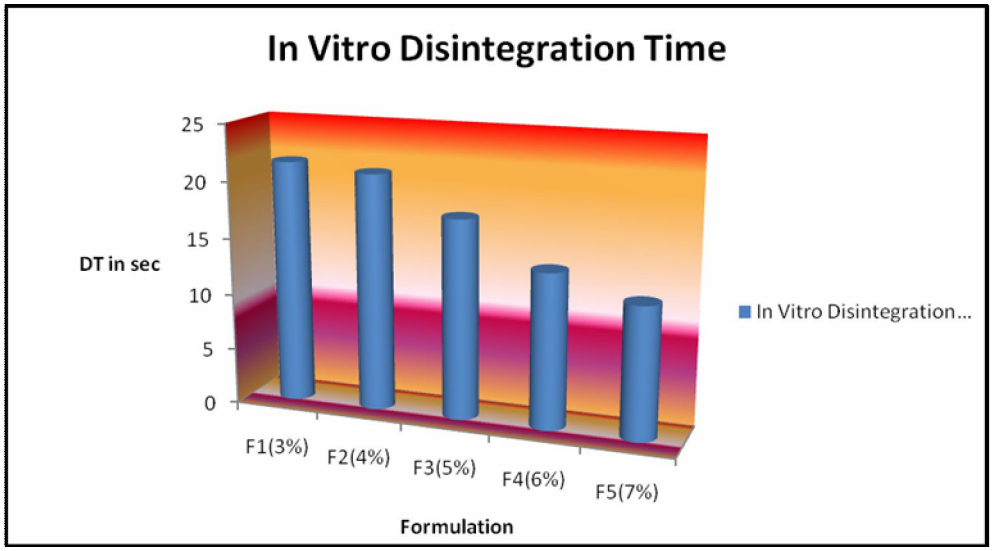


Fig. 2: Graphical representation of Isabgol concentration and In vitro Disintegration time of tablet.

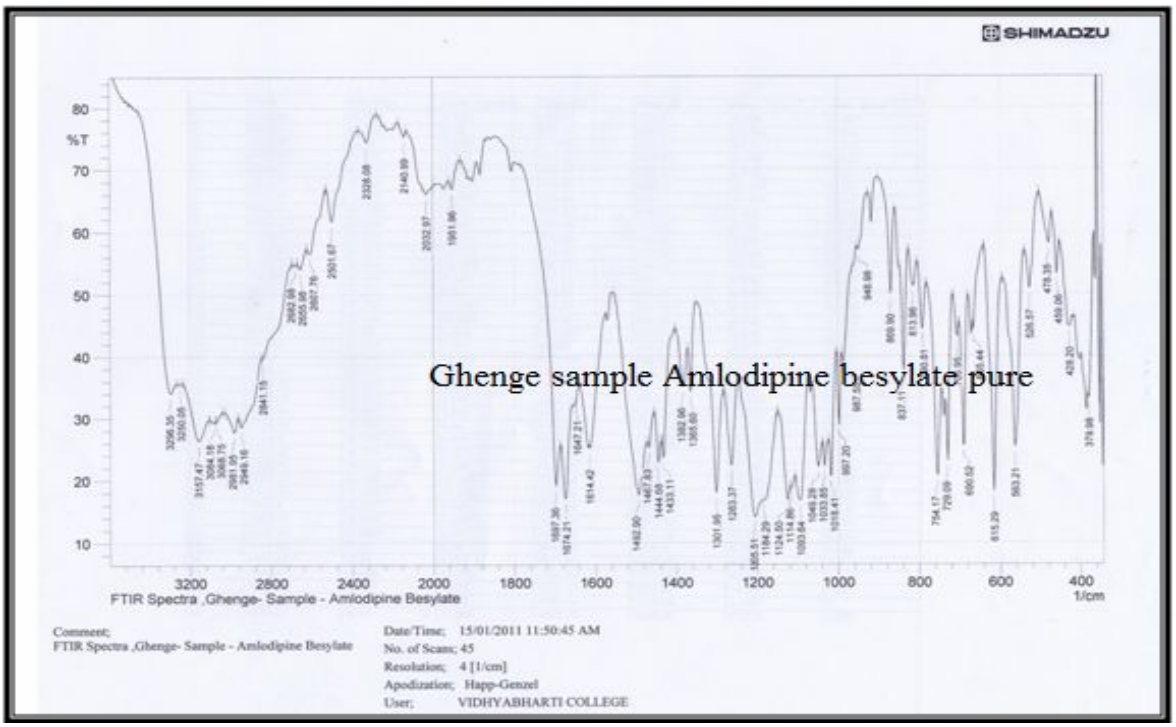


Fig-3 FTIR of Amlodipine Besylate

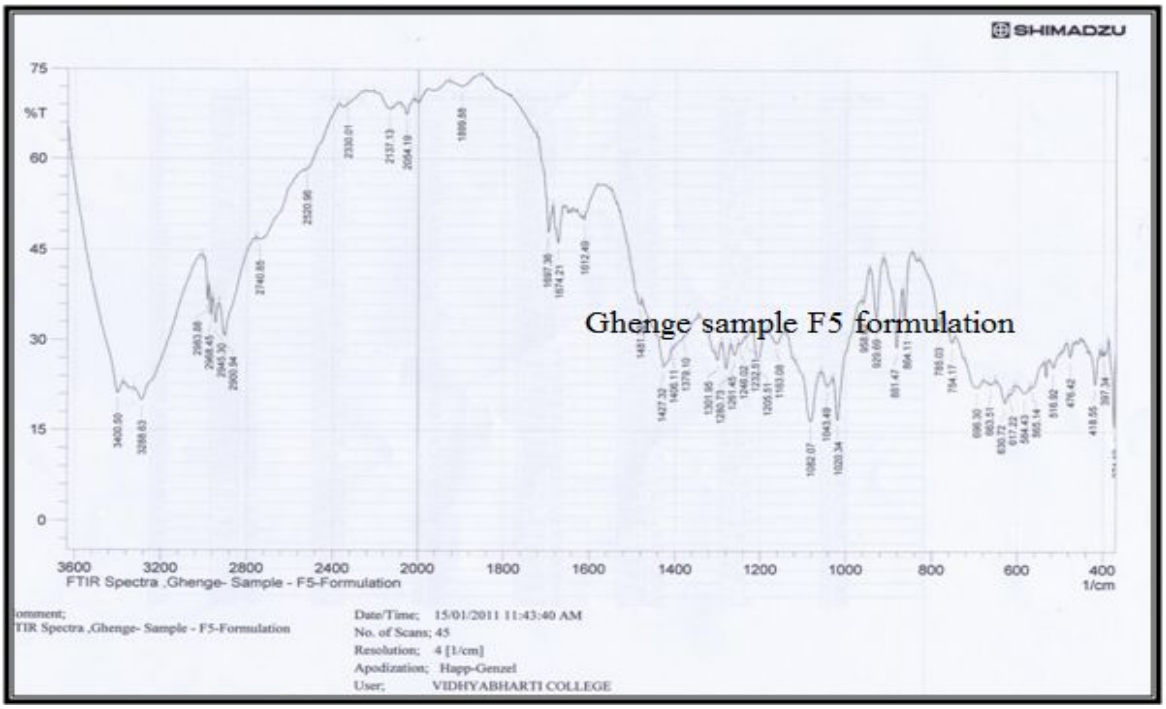


Fig-4 FTIR of Formulation F5

Results and Discussion

The values of pre-compression parameters evaluated were within prescribed limits and indicated good free flowing property is given in Table 2. The data obtained from post-compression parameters in all the formulations, friability is less than 1 %, indicated that tablets had a good mechanical resistance. Drug content was found to be in the range of 98 to 101 %, which is within acceptable limits. Hardness of the tablets was found to be in the range of 2.6-3.0 kg/cm^2. The results of weight variation, hardness, friability, wetting time and water absorption ratio were given in Table 3**.** 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 117-164 % and 8-43 sec respectively. It is observed that *in-vitro* disintegration time of tablets decreased from (21-11 sec) with increase in concentration of *plantago ovata* mucilage. The results of drug content, dissolution studies and *in-vitro* disintegration time are given in Table 4. The dissolution profiles of Amlodipine Besylate from the tablets are shown in Fig 1. Time for drug released decreased with increase in the concentrations level of *plantego ovata* mucilage. The formulations F1, F2 and F3 shows 84.96%, 87.13% and 89.82 of drug released in 16 min respectivily. Whereas F4 and F5 shows about 95.12% and 99.72% drug release in 16 min respectively. The pure drug Amlodipine Besylate exhibited characteristic absorption at 1205^{-1} cm, 1184^{-1} cm and 1589^{-1}. In formulation F5 the pure drug is with the natural superdisintegrant like *plantago ovata. Plantago ovata* is an inert substance there is no interaction. The pure drug characteristic absorption bands and formulations major characteristic absorption bands have shown all most same range. As there is no variation and shift in the position of characteristic absorption bands it can be justified there is no interaction between drug and polymer is shown in Fig 3-4.

Conclusion

The study leads us to conclude that *plantago ovata* can be successfully used as an natural superdisintegrant.

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