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DESIGN AND*IN-VITRO* EVALUATION OF FAST DISSOLVING TABLETS OF AMLODIPINE

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ABSTRACT
The objective of the study was to design and evaluate fast dissolving tablets of Amlodipine, it is a calcium channel blocker works by affecting the movement of calcium into the cells of the heart and blood vessels. This relaxes the blood vessels and lowers blood pressure, and increase the supply of blood and oxygen to the heart while reducing its workload. It has a bioavailability 64% -90%. Amlodipine showed maximum absorbance at 242nm so absorbance was measured at the same wavelength and found to obey Beer lamberts law in the concentration range of 10-40 mcg/ml. In the pre formulation study of IR spectra of pure drug with the different Super disintegrants was studied, no interactions were observed. 8 formulation of Amlodipine fast dissolving tablets were prepared by direct compression and they were examined for physical properties and appearance like hardness, thickness, weight variation, thickness, hardness, friability uniformity of drug content and *in-vitro* drug release studies. All the parameters were within the limits.[1]

KEYWORDS: Amlodipine fast dissolving tablets**,** Super disintegrants and sodium starch glycolate.

INTRODUCTION
Solid oral delivery systems do not require sterile conditions and therefore, less expensive to manufacture. A vast variety of pharmaceutical research is directed at developing new dosage forms for oral administration. Most of these efforts have focused on either formulating novel drug delivery systems or increasing the patient compliance. Tablets that rapidly dissolve upon contact with saliva in the buccal cavity could present a solution to those problems, so there is an increased interest in fast dissolving dosage forms for buccal, sublingual and oral administration. The target population for these fast-dissolving dosage form have generally been paediatric, geriatric and bedridden or developmentally disabled patients. Patients with persistent nausea, who are traveling or who have little or no access to water are good candidates for fast dissolving drug delivery system. Fast dissolving tablets are also called as mouth-dissolving tablets, melt-in mouth tablets, Oro dispersible tablets, rapimelts, porous tablets, quick dissolving tablets etc.[2 ,3]

Super disintegrants
Disintegrating agents are the substances routinely included in the tablet formulations to aid in the break-up of the compacted mass into the primary particles to facilitate the dissolution or release of the active ingredients when it is put into a fluid environment. They enhance moisture penetration and dispersion of the tablet matrix. The major function of disintegrants is to oppose the efficiency of the tablet binder and physical forces to act under compression to form the tablet. Recently new materials termed as “super disintegrants” have been developed to improve the disintegration processes. Super disintegrants are another version of super-absorbing materials with swelling properties as required. These materials swell quickly and are more effective at lower concentrations with greater disintegrating efficiency and mechanical strength. Super disintegrants are generally used at a low quantity in the solid dosage form, typically 1 - 10 % by weight relative to the total weight of the dosage unit. Generally, one gram of super disintegrant absorbs 10-40 g of water or aqueous medium. After absorption, swelling pressure and isotropic swelling of the super disintegrant particles create stress concentrated areas where a gradient of mechanical properties will exist due to which whole structure will break apart.[4,5]

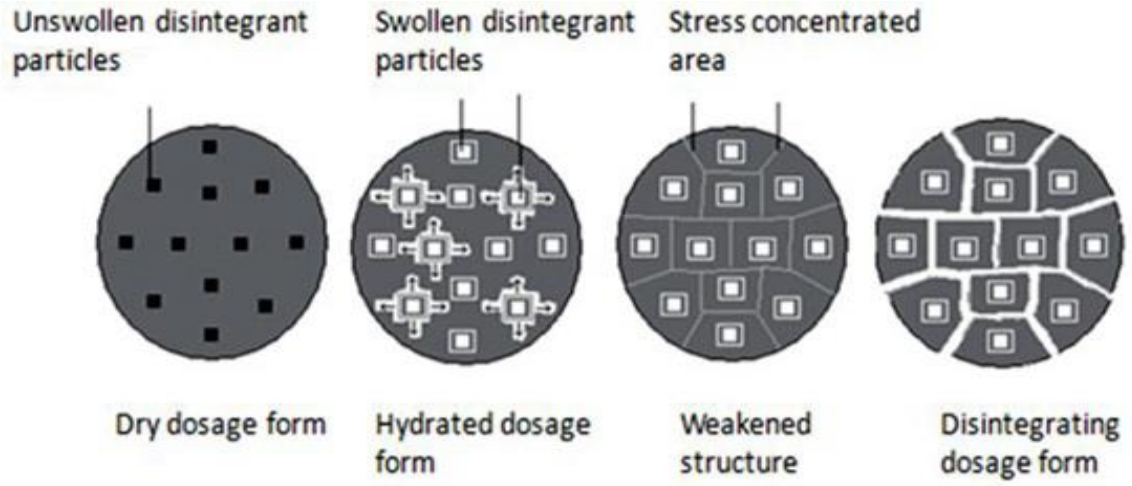

Figure 1: Super disintegrants breaking the tablet structure.

MATERIALS AND METHODS

Amlodipine was obtained from KAPL Bangalore. All other chemicals were obtained from laboratory grade.

METHODS

PREPARATION OF FAST DISSOLVING TABLETS OF AMLODIPINE

Accurately weighed quantities of super disintegrants and MCC were taken in a mortar and mixed geometrically. Then accurately weighed quantity of Mannitol was added and Amlodipine mixed in a mortar and pestle. The powder was passed through sieve no 40. To this Magnesium stearate and talc was added and mixed for 5 minutes. The mixture equivalent to 200 mg was compressed into tablets[6,7]

Table 1: Composition of fast dissolving tablets of Amlodipine.

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8
Amlodipine	10	10	10	10	10	10	10	10
SodiumstarchGlycolate	5	10	15	20	---	-----	----	------
Crospovidone	------	------	-----	-----	5	10	15	20
Mannitol	150	150	150	150	150	150	150	150
Micro Crystalline Cellulose	30	25	20	15	30	25	20	15
Magnesium stearate	3	3	3	3	3	3	3	3
Talc	2	2	2	2	2	2	2	2

Figure 2: Fast dissolving tablets of Amlodipine.

Standard graph of Amlodipine in phosphate buffer 6.8 pH

A stock solution of 1mg/ml of Amlodipine was prepared by dissolving 10 mg of drug with100 ml of Phosphate buffer 6.8 pH. The stock solution was serially diluted to get solution in the range of 10-50µg/ml and λ max of the solution was found outby scanning from 200-400 nm. The λ max was found to be 242 nm.

DRUG-EXCIPIENT COMPATIBILITY STUDIES

Fourier Transform Infrared (FTIR) Spectroscopy

The Fourier transform infrared (FTIR) spectra of samples were obtained using FTIR spectrophotometer (Perkin Elmer). Pure drug, individual polymers and optimised formulations were subjected to FTIR study. About 2–3 mg of sample was mixed with dried potassium bromide of equal weight and compressed to form a KBr disk. The samples were scanned from 400 to 4000 cm^{-1}.

Pre-compression parameters

Angle of Repose: The angle of repose is the constant, three-dimension angle (relative to horizontal base) assumed by a cone like pile of material formed by any of several different methods. When the angle of repose exceeds 50degrees, the flow is rarely accepted for manufacturing purpose.

Bulk Density: The bulk density was determined by transferring the accurately weighed sample of powder to the graduate cylinder. The initial volume and weight was noted. Ratio of weight of the sample was calculated by using the following formula.

Bulk Density =Mass /Bulk volume.

Tapped Density: Weighed powder sample was transferred to a graduated cylinder and was placed on the tap density apparatus, was operated for fixed number of taps(100).The tapped density was determined by the following formula.

Tapped Density =Mass/Tapped volume.

Percentage compressibility: Based on the apparent bulk density and tapped density, the percentage compressibility of the bulk drug was determined by the following formula.

% Compressibility=Tapped density-Bulk density×100/ Tapped density.

Hauser's Ratio: It is measured by the tapped density to bulk density.

Hauser's Ratio= Tapped density/Bulk density

POST COMPRESSION PARAMETERS

Tablet thickness

Randomly 5 tablets were taken from each formulation trial batch and their thickness was determined by using screw gauge.

Weight variation test

20 tablets were randomly selected from each formulation trial batch and their average weight was calculated using digital balance. Individual weight of each tablet was also calculated using the same and compared with the average weight.

Measurement of tablet hardness

Hardness of 10 tablets was found using Monsanto hardness tester, mean and standard deviation were computed and reported. It is expressed in $kg/cm.^2$

Friability

10 tablets were weighed and placed in Roche friabilator where the tablets were exposed to rolling and repeated shocks resulting from free falls within the apparatus. The Friabilator was operated at 25 rpm for 4 mins. After 100 revolutions, tablets were removed, deducted and weighed again. The friability was determined as the percentage loss in weight of the tablets.

***In vitro* Drug Release Studies**

The *in vitro* drug release study was performed by using USP Type II dissolution apparatus using900ml of phosphate buffer 50 rpm37±0.5ºCsampling volume 5ml was withdrawn at predetermined time intervals samples (5 ml) were collected and replenished with same volume of fresh media. The drug content in the samples was estimated using UV-spectrophotometer at242 nm.

Water absorption ratio

A piece of tissue paper folded twice was placed in petri plate containing 6 ml of water. A tablet was placed on it and the time required for complete wetting was measured. The wetted tablet was weighed. Water absorption ratio was measured R was determined using following formula.[8,910]

R=100(Wa-Wb)/Wb

Wb-Weight of tablets before absorption

Wa-Weight of tablets after absorption

RESULTS AND DISCUSSION

CALIBRATION CURVES OF AMILODIPINE.

Preparation of Amlodipine standard stock solution (100 µg/ml) pH 6.8phosphate buffer.

Standard stock solution of Amlodipine was prepared by dissolving accurately weighed10 mg of Amlodipine in little quantity of phosphate buffer 6.6 pH in a 100 ml volumetric flask. The volume was then made up to 100 ml using pH 6.6 phosphate buffer to obtained the solution of 100 µg/ml.

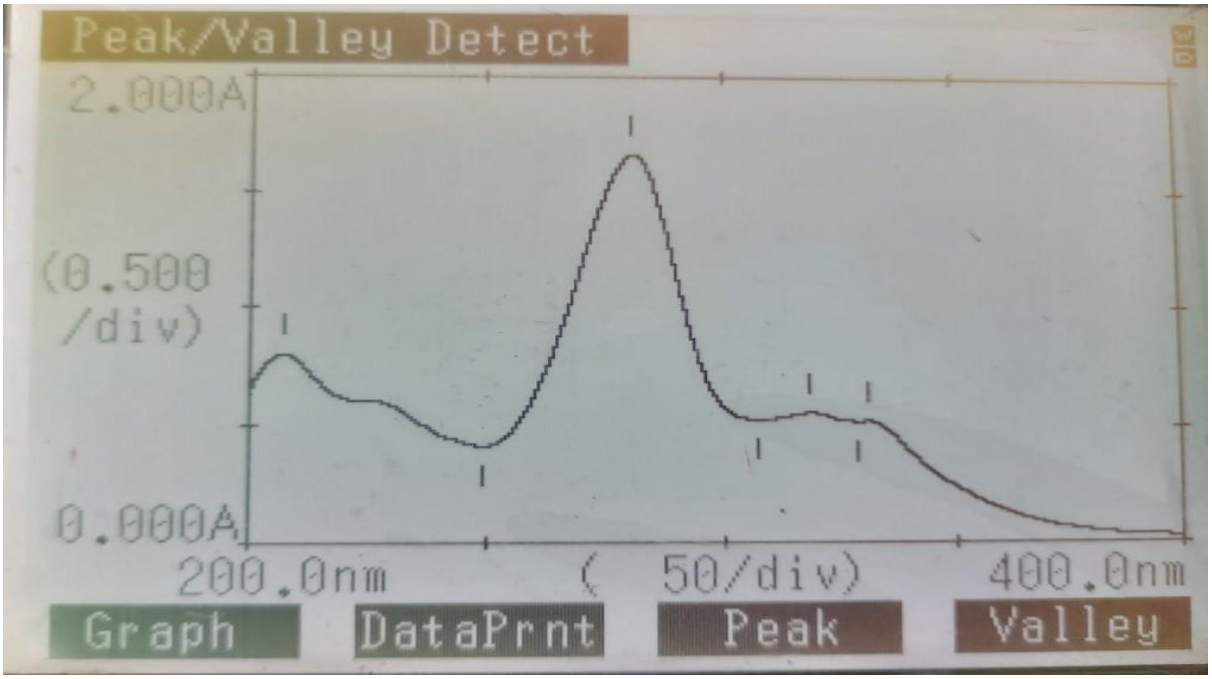

Figure 3: λ max of Amlodipine in phosphate buffer 6.8 pH.

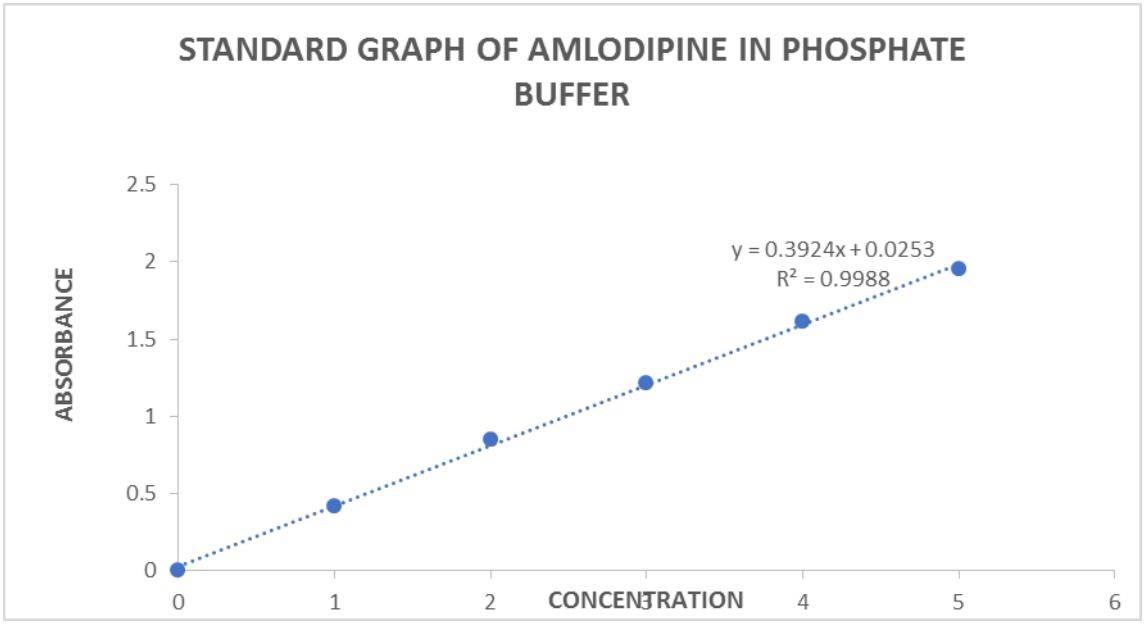

Figure 4: Calibration curve of Amlodipine in pH 6.8 phosphate buffer.

Amlodipine was suitable diluted using phosphate buffer having pH 6.8 to get 1 µgm to 10 µgm/ml concentration and prepared samples were scanned in the UV range of 200-400 nm using phosphate buffer pH 6.8 as a blank. The λmax was found to be 24 2nm respectively.

DRUG-EXCIPIENT COMPATIBILITY STUDIES

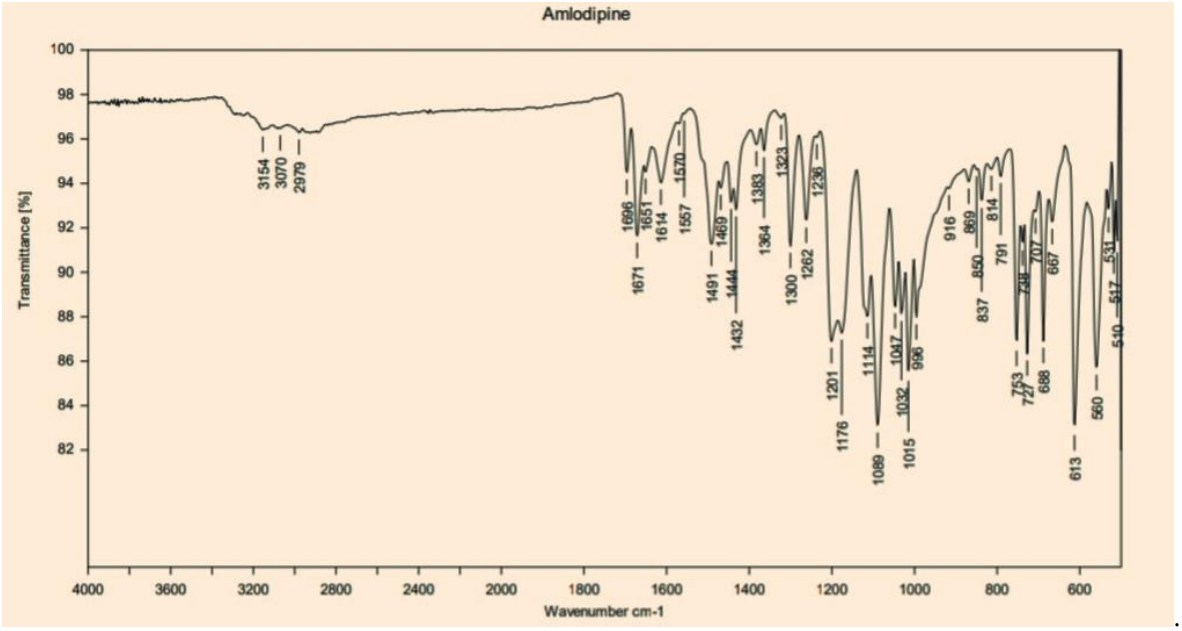

Figure 5: FTIR spectra of pure drug.

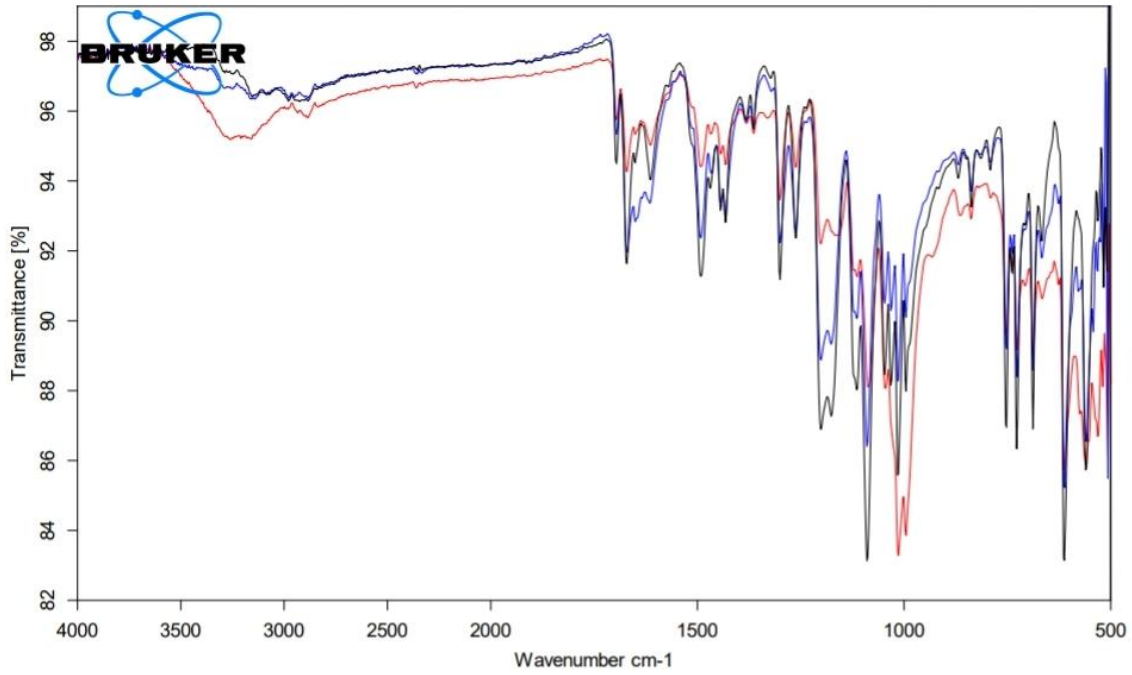

Figure 6: FTIR spectra of pure drug and Super disintegrants used in formulations.

Fourier Transform Infrared (FTIR) Spectroscopy

Potential chemical interaction between drug and polymer may change the therapeutic efficacy of the drug. To investigate the possibility of chemical interaction between drug and polymer FTIR spectra of pure Amlodipine and Super disintegrants used in formulations were analysed over the range 400–4000 cm^{-1}. No interactions were observed. Hence the drug and the super disintegrants were compatible.

Table 2: Micrometric properties.

Formulationcode	Angle of repose (°)	Bulk density (gm/ml)	Tapped density(gm/ml)	Carr'sIndex (%)	Hauser's ratio
F1	28.60	0.316	0.421	24.94	1.166
F2	30.464	0.323	0.461	29.93	1.427
F3	31.32	0.315	0.446	29.37	1.415
F4	30.96	0.320	0.420	23.80	1.312
F5	38.55	0.323	0.417	22.54	1.291
F6	30.64	0.255	0.422	39.57	1.654
F7	28.60	0.410	0.540	24.07	1.317
F8	26.60	0.345	0.452	23.67	1.310

Precompression parameters revealed that angle of repose was in the range of 26.60-38.55.Bulk density was in the range of 0.255-0.410 gm/ml, tapped density in range of 0.420-0.540 gm/ml and compressibility in the range of 1.291-1.654%.Which showed all the parameters were in acceptable limits.

Table 3: Physical parameters of Amlodipine fast dissolving tablets.

Formulation code	Weight variation (mg)	Hardness (kg/cm^2)	Thickness (mm)	Friability (%)	Assay (%)
F1	200.38	3.1	3.00	0.53	96.23
F2	201.52	2.8	3.12	0.50	99.65
F3	199.23	3.5	3.09	0.96	96.12
F4	202.6	4.0	3.15	0.97	95.44
F5	200.19	2.8	3.12	0.49	97.23
F6	201.71	2.6	3.08	0.52	96.63
F7	200.44	2.8	3.50	0.51	97.44
F8	201.65	3.6	3.46	0.52	96.98

Post compression parameters were in the range of Weight variation 119.25-201.65mg, hardness in the range of 2.6-4 $kg/cm^{2,}$ Thickness in the range of 3-3.5mm,frability ranging from 0.49-0.97% and content uniformity in range of 95.44-99.65%, indicating uniformization dispersion of the drug and F2 showed the highest content uniformity.

Table 4: Water absorption ratio of Amlodipine fast dissolving tablets.

Formulation code	Disintegration time (sec)	Water absorption ratio	Wetting time (sec)
F1	20	35.48	10
F2	15	33.33	13
F3	25	30.00	12
F4	21	32.25	13
F5	24	45.71	17
F6	23	63.33	21
F7	24	42.85	14
F8	22	44.44	16

Disintegration time was in the range of 15- 25 and F2 showed the less disintegration, water absorption ratio was in the range of 33.33-63.33 and wetting time in the range of 10-21 sec.

Figure7: Water absorption ratio of Amlodipine fast dissolving tablets.

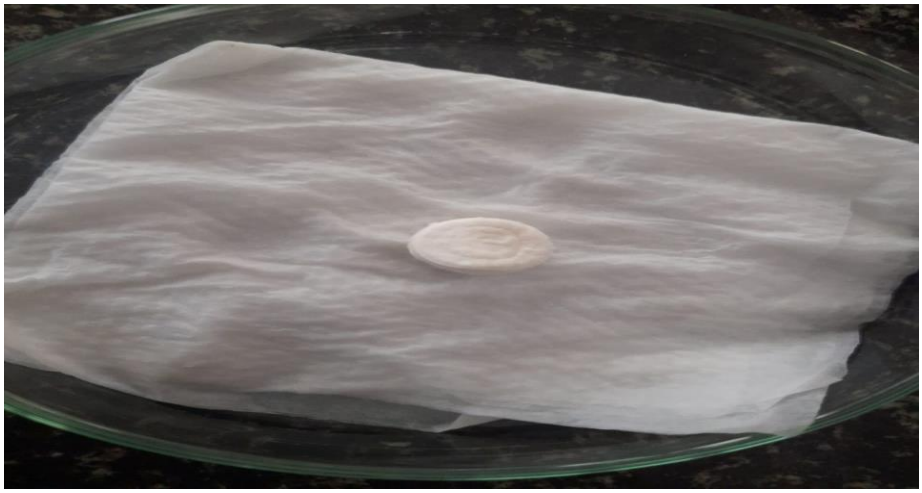

Figure 8: Water absorption ratio of Amlodipine fast dissolving tablets after complete wetting.

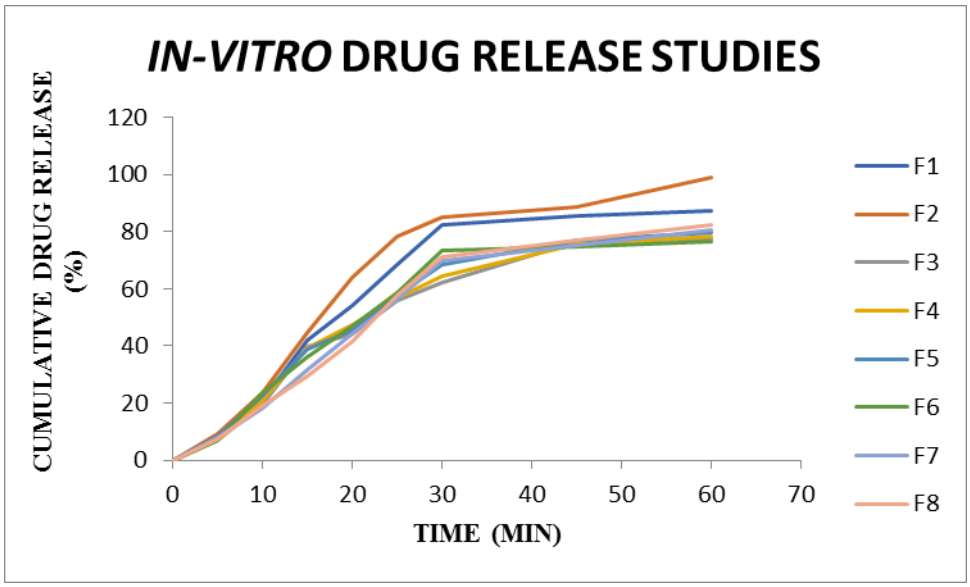

Figure 9: *In-vitro* drug release study.

1. *In-vitro* dissolution studies were carried out by phosphate buffer (6.8 pH) solution as dissolution medium and dissolution studies were carried out for 60 minutes for each formulation and calculated for its %CDR to find out the amount of drug release in each formulation. F2 showed highest %CDR of 99.2 % at the end of 60^{th} minute among the other formulations.

CONCLUSION

Fast dissolving tablets of Amlodipine were successfully prepared by using different super disinterdents by simple direct compression method. FTIR studies showed no incompatibility between drug, super disintergents and various excipients used in the formulations. Formulated tablets gave satisfactory results for various evaluation parameters like tablet dimensions, hardness, weight variation, friability, content uniformity angle of repose, bulk density, Carr's index, Hausner's ratio and post compression parameters like hardness, thickness, friability, weight variation, water absorption ratio, drug content, *in-vitro* disintegration time and *in-vitro* dissolution studies.

The observations showed that all the FDT formulations were accepted with reasonable limits of standards required for fast dissolving tablets. The study reveals that the formulations prepared by Crospovindone was best than Sodium starch glycolate. Formulations prepared by Crospovindone F2 was the best formulation. The study revealed that super disintegrants used were effective in low concentration level.

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