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Formulation & Evaluation of Fast Dissolving Tablets of Amlodipine Besylate by Using Co-Processed Superdisintegrants

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Authors' contributions

This work was carried out in collaboration between all authors. Author JTN designed the study, performed the statistical analysis, wrote the protocol, and wrote the first draft of the manuscript. Authors VVP, VDT and TA managed the analyses of the study. Authors MHK and CRV managed the literature searches. All authors read and approved the final manuscript.

Research Article

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ABSTRACT

Aims: To formulate fast dissolving tablets of amlodipine besylate using co-processed superdisintigrant and evaluate the properties of fast dissolving tablets.
Study Design: Formulation, evaluation of fast dissolving tablets of amlodipine besylate.
Place and Duration of Study: Department of Quality Assurance S. N. D. College of Pharmacy Babhulgoan Yeola Dist Nashik 423401, between July 2012 to February 2013.
Methodology: In the present study, novel co-processed superdisintegrants were developed by solvent evaporation method using crospovidone and sodium starch glycolate in different ratios (1:1, 1:2 1:3 2:1, 3:1) in the fast dissolving tablet formulations. Drug and the developed excipients were characterized for compatibility studies with FTIR and DSC. The co-processed superdisintigrant mixture was evaluated for angle of repose, Carr's index and Hausner's ratio in comparison with physical mixture of

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superdisintegrants. Fast dissolving tablets of Amlodipine Besylate were prepared using co-processed superdisintegrants and evaluated for pre-compression and post-compression parameters. Effect of co-processed superdisintegrants (crospovidone and sodium starch glycolate) on wetting time, disintegrating time, drug content, *in-vitro* release, and stability parameters have been studied.

Results: The angle of repose of the developed excipients was found to be < 30^0 Compressibility (%) index in the range of 13.14 to 14.63 % and Hausner's ratio in the range of 1.15-1.19. The prepared tablets were characterized by FTIR and DSC Studies there was no change in the result. Based on *in-vitro* dispersion time (approximately 40 sec), promising formulation CP5 was tested for *in-vitro* drug release pattern in phosphate buffer pH 6.8.

Conclusion: Among the designed formulations, the formulation (CP5) containing co-processed superdisintegrant (3:1 mixture of crospovidone and sodium starch glycolate) emerged as the overall best formulation based on drug release characteristics in phosphate buffer pH 6.8. From this study, it can be concluded that dissolution rate of amlodipine besylate could be enhanced by tablets containing co-processed superdisintegrant.

Keywords: Co-processed mixture; sodium starch glycolate; crospovidone; amlodipin besylate; FDT.

1. INTRODUCTION

Tablets have remained the most common dosage form by which medicaments are usually administered to patients because of their advantages over the other dosage forms. Tablet dosage forms are the most popular and preferred drug delivery systems in terms of precision of unit dose, low cost, patient compliance, and good physical and chemical stability. Tablets account for 70% - 80% of all pharmaceutical dosage forms [1].

Hypertension is becoming an important public health challenge worldwide. Hypertension is one of the main risk factors for cardiovascular diseases, which is one of the leading causes of death in developed countries [2]. The relationship between blood pressure and risk of cardiovascular disease is continuous, consistent and independent of other risks. The higher the blood pressure, the greater is the chance of ischemic heart disease, stroke, heart failure and kidney diseases. Therefore prevention, detection, treatment and control of hypertension should receive high priority [3]. Many patients have difficulty to swallow tablets and hard gelatin capsules. This results in high incidence of noncompliance and ineffective therapy [4].There is unavailability of water during travelling, to overcome these problems fast dissolving tablet is emerged. FDT dissolves rapidly in the saliva without the need for water, faster the dissolution and provide quick onset of action. The bioavailability of drug is significantly enhanced by avoiding first pass hepatic metabolism than conventional tablets [5].

Amlodipine is a dihydropyridine calcium antagonist (calcium ion-channel blocker) that inhibits the transmembrane influx of calcium ions into vascular smooth muscle and cardiac muscle. It binds to both dihydropyridine and non dihydropyridine binding sites. The contractile processes of cardiac muscle and vascular smooth muscle are dependent upon the movement of extra cellular calcium ions into these cells through specific ion channels. Amlodipine inhibits calcium ion influx across cell membranes selectively, with a greater effect

on vascular smooth muscle cells than on cardiac muscle cells [6]. Amlodipine is an ionized compound having ionization value 8.6 (pKa = 8.6) [7].

The bioavailability of amlodipine besylate, the functionality of excipients is improved by co-processed method [8].

Co-processing is based on the novel concept of two or more excipients interacting at the sub particle level, the objective of which is to provide a synergy of functionality improvement as well as masking the undesirable properties of individual Co-processing excipients lead to the formulation of excipient granules with superior properties, compared with physical mixtures of components or individual components, like improved flow properties, improved compressibility, better dilution potential, fill weight uniformity, and reduced lubricant sensitivity [9,10]. Several co-processed superdisintegrants are commercially available: Ludipress (lactose monohydrate, polyvinylpyrrolidone and crospovidone), Starlac (lactose and maize starch), Starcap 1500 (corn starch and pregelatinized starch), Ran Explo-C (microcrystalline cellulose, silica and crospovidone), Ran Explo-S (microcrystalline cellulose, silica and sodium starch glycolate), PanExcea MH300G (microcrystalline cellulose, hydroxy propyl methyl cellulose and crospovidone) [11].

In present study, the preparation and evaluation of FDT by using co processed superdisintegrants containing crospovidone and sodium starch glycolate was studied. The reasons for selection of crospovidone are high capillary activity, pronounced hydration capacity and little tendency to form gels [12,13,14]. Sodium starch glycolate has high swelling capacity [15]. The concept of formulating fast dissolving tablets (FDT) of amlodipin besylate (anti-hypertensive) using co-processed superdisintegrants helps to increase the water uptake with shortest wetting time and thereby decrease the disintegration time of the tablets by simple and cost effective direct compression technique.

2. MATERIALS AND METHODS

2.1 Materials

Amlodipine besylate is procured by wockhardt Aurangabad, crosspovidone (polyplasdone) and sodium starch glycolate are gifted by Sai Tech Lab. Sinner (Nasik), Microcrystalline Cellulose, Manitol Isopropyl alcohol procured by our college.

2.2 Methods

2.2.1 Preparation of co-processed superdisintegrants

The co-processed superdisintegrants were prepared by solvent evaporation method. Crospovidone and sodium starch glycolate (in the ratio of 1:1, 1:2, 1:3, 2:1, 3:1) were mixed together with 10 ml of isopropyl alcohol. The contents of beaker (250 ml capacity) were mixed thoroughly and stirring continue till most of isopropyl alcohol evaporated. The wet coherent mass was granulated through # 44 mesh sieve. The wet granules were dried in a hot air oven at 60ºC for 20 minutes. The dried granules were sifted through # 44 mesh sieves and stored in airtight container till further use [16,17,18] (Table 1).

Table 1. Different batches of superdisintigrants

Code of Mixture	PM1	PM2	PM3	PM4	PM5	CP1	CP2	CP3	CP4	CP5
Crospovidone	1	1	1	2	3	1	1	1	2	3
SSG	1	2	3	1	1	1	2	3	1	1

PM - Physical Mixture CP - Co-processed Superdisintegrants of Cp and SSG in different ratios (1:1, 1:2, 1:3, 2:1,3:1), Cp – Crosspovidone, SSG – Sodium Starch Glycolate

2.3 Preparation of Fast Dissolving Tablets

Fast dissolving tablets of amlodipine besylate were prepared by direct compression. All the ingredients (except granular directly compressible excipients) were passed through # 60 mesh separately. Then the ingredients were weighed and mixed in geometrical order and compressed into tablets of 150 mg using LAB PRESS compression machine with 12 compression stations and 8 mm round flat punches are used for tablet compression (Table 2) [19].

Table 2. Formulations of amlodipin besylate FDT prepared by direct compression method

Ingredients	Formulation code										
	CP0	**PM 1**	**PM 2**	**PM 3**	**PM 4**	**PM 5**	**CP 1**	**CP 2**	**CP 3**	**CP 4**	**CP 5**
Amlodipin Besylate	5	5	5	5	5	5	5	5	5	5	5
CP(Crospovidone + SSG)	-	6	6	6	6	6	6	6	6	6	6
Aspartame	3	3	3	3	3	3	3	3	3	3	3
Magnesium stearate	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Talc	3	3	3	3	3	3	3	3	3	3	3
Flavour	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Microcrystalline cellulose	30	30	30	30	30	30	30	30	30	30	30
Mannitol	106	100	100	100	100	100	100	100	100	100	100
Total weight (mg)	150	150	150	150	150	150	150	150	150	150	150

2.4 Evaluation of Amlodipin Besylate Fast Dissolving Tablets

2.4.1 Pre compression Evaluation Parameters

2.4.1.1 Angle of repose

Angle of repose is defined as the maximum angle possible between the surface of a pile of the powder and horizontal plane. It is calculated by using following formula.

$$\mathbf{Tan\ \Theta = h / r}$$
$$\mathbf{\Theta = \tan^{-1}(h/r)}$$

Where, Θ is the angle of repose
h is height of pile
r is radius of the base of pile

2.4.1.2 Bulk density

Bulk density is defined as the mass of a powder divided by the bulk volume. Loose bulk density (LBD) and tapped bulk density (TBD) were determined. A quantity of accurately weighed powder was introduced into a *25* ml measuring cylinder. After the initial volume was observed, the cylinder was allowed to fall under its own weight onto a hard surface from the height of 2.5 cm at 2 sec interval. The taping was continued until no further change in volume was noted. LBD and TBD were calculated using following formula;

$$\text{LBD} = \frac{\text{Weight of the powder}}{\text{Volume of the packing}}$$

$$\text{TBD} = \frac{\text{Weight of the powder}}{\text{Tapped volume of the packing}}$$

2.4.1.3 Tapped density

The measuring cylinder containing a known mass of blend was tapped for a fixed time. The minimum volume (Vt) occupied in the cylinder and the weight (M) of the blend was measured. Electrolab Tap Density Tester USP ETD-1020 is used for determination of tapped density. The tapped density (pt) was calculated using the following formula.

$$\rho t = \frac{M}{Vt}$$

2.4.1.4 Hausner ratio

Hausner ratio is an indirect index of ease of power flow. It is calculated by the following formula.

$$\text{Hausner Ratio} = \frac{\rho t}{\rho d}$$

Where ρ_t is tapped density and ρ_d is bulk density. Lower Hausner ratio (<1.25) indicates better flow properties than higher ones (>1.25).

2.4.2 Post compression evaluation parameters

2.4.2.1 Weight variation

Twenty tablets were selected randomly from each formulation and weighed individually using a Shimadzu digital balance (BL-220H). The individual weights were compared with the average weight for the weight variation [20].

2.4.2.2 Thickness variation

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

2.4.2.3 Hardness and friability

Hardness of the tablets was measured using the Monsanto Hardness Tester (Pharmalab, Ahmedabad, India). The friability of a sample of twenty tablets was measured using Roche friabilator (Pharma lab, Ahmedabad, India). Pre-weighed tablets were placed in the plastic chamber of friabilator attached to a motor revolving at a speed of 25 rpm for 4 min. The tablets were then dusted, reweighed and percentage weight loss (friability) was calculated.

2.4.2.4 Fourier transform infrared spectroscopy (FTIR)

The samples of amlodipine besylate and co-processed mixture of crosspovidone and sodium starch glycolate are scanned by using Model ALPHA Brucker ECO-ATR. The scanning range was from 4000-400 cm^{-1}.

2.4.2.5 Drug content uniformity

For the content uniformity test, ten tablets were weighed and pulverized to a fine powder, a quantity of powder equivalent to 10 mg of amlodipin besylate was extracted into distilled water and liquid was filtered (0.22 µm membrane filter disc. The amlodipin besylate content was determined by measuring the absorbance at 235.7 nm (using UV-vis spectrophotometer, Shimadzu 1700) after appropriate dilution with distilled water. The drug content was determined using standard calibration curve. The mean percent drug content was calculated as an average of three determinations [21].

2.4.2.6 In vitro dispersion time

One tablet was placed in a beaker containing 10 ml of pH 6.8 phosphate buffers at 37 ± 0.5ºC and the time required for complete dispersion was determined.

2.4.2.7 Wetting time and water absorption ratio (R)

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:

$$\mathbf{R = 100 \times (Wa - Wb)/ Wb}$$

Where;

Wb and **Wa** were tablet weights before and after water absorption, respectively.

2.4.2.8 In vitro drug release study

In vitro dissolution studies of the promising fast dissolving tablets of amlodipin besylate, all formulations were performed according to USP XXIII Type-II dissolution apparatus employing a paddle stirrer at 50 rpm using 900 ml of pH 6.8 phosphate buffers at 37±0.5ºC as dissolution medium. One tablet was used in each test. Aliquots of the dissolution medium (5 ml) were withdrawn at specific time intervals (1, 2, 3, 4, 5, 10, 15, 20, 25 & 30 min) and replaced immediately with equal volume of fresh medium. The samples were analyzed for drug content by measuring the absorbance at 237.5 nm. Drug concentration was calculated

from the standard calibration curve and expressed as cumulative percent drug dissolved. The release studies were performed in replicates of three [22].

2.4.2.9 Stability studies

The promising formulations were subjected to short term stability study by storing the formulations at 40ºC/75% RH up to three month. The formulations **PM1 PM5 CP1 CP5 w**ere selected. After one month the tablets were again analyzed for the hardness, friability, drug content uniformity and dispersion time. The increase in the disintegration time was observed in case of tablets prepared with physical mixture method. This may be due to increase in the hardness of the tablets during storage. Decrease in the disintegration time was observed in tablets prepared by co-processed mixture method. No change was observed in the disintegration time and hardness of tablets prepared by other technique. No significant change was observed in the drug content of all formulation.

3. RESULTS AND DISCUSSION

3.1 Drug Polymer Interaction Study

IR spectra for pure drug and formulations were recorded in an infrared (IR) spectrophotometer (Model ALPHA Brucker ECO-ATR) FTIR studies revealed that amlodipine besylate bands at 3016 cm–1 due to C-H stretching vibration and a band at 2980 cm–1 due to Ar-H stretching, and characteristics bands at 1696 N-H stretching and 1653 cm–1 assigned to C=C stretching.C-O stretching at 1308 cm-1 and C-Cl stretch at 754 cm-1.No significant shifts of reduction in intensity of the FTIR bands of amlodipine besylate were observed as shown in Fig. 1.

DSC analyses were performed in order to evaluate possible solid-state interactions between the components and, consequently, to assess the actual drug-excipient compatibility in all the examined formulations. The thermal curves of pure components and those of some representative ternary systems are shown in Figs. 2 & 3. Thermograms of pure amlodipine besylate showed sharp endothermic peak at 217.95ºC (Fig. 2). Similar peaks were obtained in the prepared drug-polymer mixtures at 213.3ºC (Fig. 3). This clearly indicated the nil drug polymer interaction.

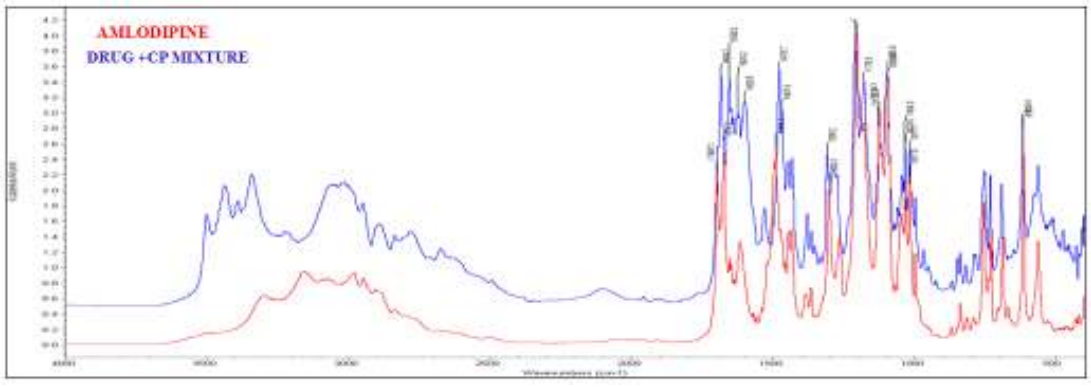

Fig. 1. Joint spectra of drug and CP mixture

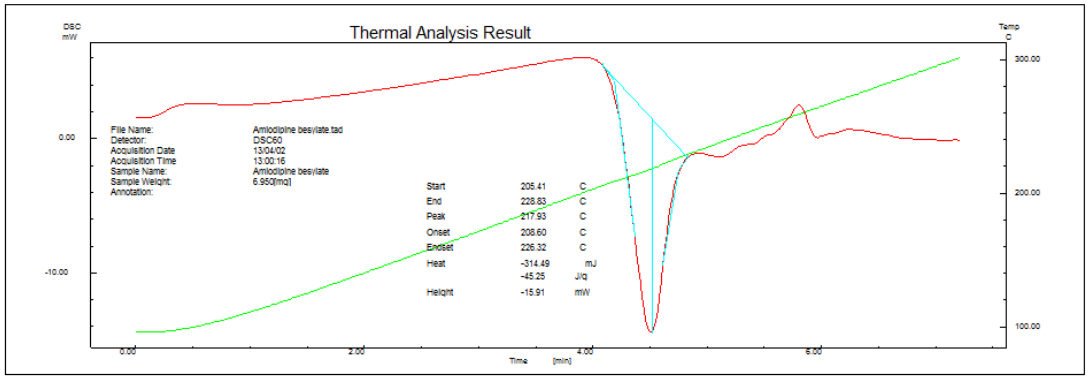

Fig. 2. DSC of pure drug

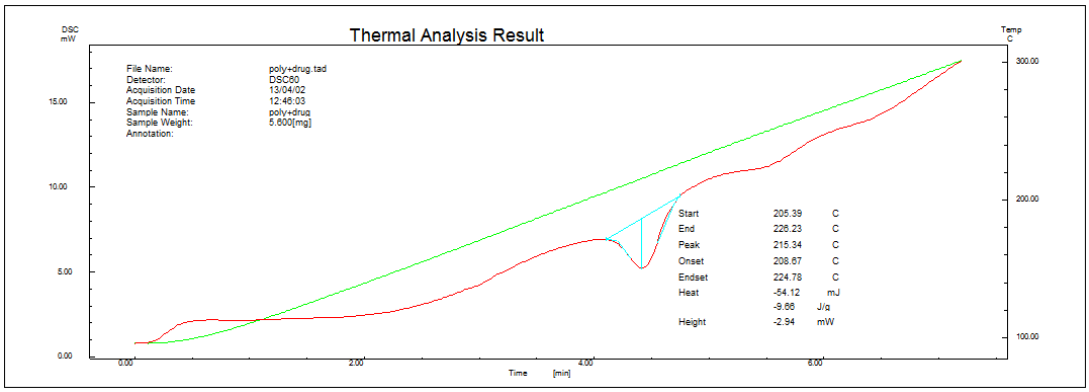

Fig. 3. DSC of drug + polymer

3.2 Pre Compression Studies

A) Angle of repose (Ɵ):

The data obtained from angle of repose for superdisintigrant mixture and all the formulations were found to be in the range of 21.53333±0.85049to 29.22±0.416 and 22.5±0.926 to 29.5 ±1.023 respectively. All the formulations prepared by both the methods showed the angle of repose less than 30º, which reveals good flow property (Tables 3 & 4).

B) Bulk density:

Loose bulk density (LBD) for superdisintigrant blend and formulation varied from 0.353±0.035119 gm/cm^3 to 0.448±0.0415 gm/cm^3 and 0.45±0.031to 0.47±0.012 respectively. Tapped bulk density (TBD) of superdisintigrant and the entire formulation 0.406667±0.025166 gm/cm^3 to 0.52±0.01 gm/cm^3 and 0.52±0.022 to0.54±0.030 (Tables 3 & 4).

Table 3. Pre-compression parameters of co-processed and physical mixture of superdisintegrants

Formulation code	Parameter				
	Bulk density (g/cc)	Tapped density (g/cc)	Angle of repose (degree)	Carr's index (percent)	Hausner's Ratio
PM1	0.367 ±0.017	0.467 ±0.035	29.22 ±0.416	15.07 ±0.39	1.20 ±0.030
PM2	0.41 ±0.036	0.467 ±0.035	26.93 ±0.668	13.67 ±0.5577	1.177 ±0.033
PM3	0.448 ±0.0415	0.48 ±0.02	25.7 ±0.721	14.233 ±0.557	1.18 ±0.0123
PM4	0.4403 ±0.026274	0.513 ±0.028	26.017 ±0.8285	13.967 ±0.5032	1.178 ±0.0131
PM5	0.4363 ±0.0047	0.52 ±0.01	26.85 ±0.82636	14.3 ±0.655744	1.178 ±0.0239
CP1	0.38 ±0.02	0.453 ±0.03519	24.85 ±0.377492	12.477 ±0.3659	1.27 ±0.0205
CP2	0.41 ±0.0366	0.45 ±0.0366	23.8 ±0.3605	15.006 ±0.339	1.207 ±0.03459
CP3	0.353 ±0.0359	0.4067 ±0.02516	23.467 ±0.60271	13.6 ±0.556776	1.218 ±0.024
CP4	0.35 ±0.04	0.4633 ±0.0452	22.673 ±0.821	13.43 ±0.5032	1.177 ±0.0146
CP5	0.4467 ±0.0450	0.503 ±0.041633	21.53 ±0.85049	13.633 ±0.503322	1.194 ±0.010583

Table 4. Pre-compression parameters of amlodipin besylate FDT formulations prepared by direct compression method

Formulation code	Parameter				
	Bulk density (g/cc)	Tapped density (g/cc)	Angle of repose(degree)	Carr's index (percent)	Hauser's Ratio
CP 0	0.47±0.030	0.53±0.031	29.5±1.023	12.90±2.985	1.177± 0.019
PM 1	0.45±0.031	0.53±0.025	29.14±1.025	14.81±1.56	1.172± 0.021
PM 2	0.46±0.016	0.54±0.024	27.45±0.956	14.52±1.25	1.172± 0.025
PM 3	0.47±0.021	0.55±0.031	25.15±0.911	12.96±1.364	1.169 ±0.027
PM 4	0.47±0.012	0.54±0.026	27.5±0.892	14.02±1.89	1.152±0 .015
PM 5	0.46±0.016	0.54±0.020	26.7±1.012	12.96±1.715	1.165± 0.013
CP 1	0.47±0.024	0.54±0.030	24.15±1.123	13.23±1.62	1.159± 0.014
CP 2	0.465±0.020	0.53±0.024	23.30±1.002	14.51±1.31	1.142 ±0.019
CP 3	0.47±0.024	0.54±0.025	23.05±0.856	13.21±1.65	1.162± 0.017
CP 4	0.46±0.021	0.52±0.022	22.8±0.752	13.22±1.82	1.152±0 .019
CP 5	0.47±0.26	0.53±0.019	22.5±0.926	13.11±1.62	1.155±0. 021

C) Hausner's ratio:

Hausner's ratio of superdisintigrant and entire formulation showed between 1.177133±0.014162 to 1.2158±0.024301 and 1.142±0.019 to 1.177±0.019 respectively which indicates better flow properties.

D) Carr's consolidation index:

The results of Carr's consolidation index or compressibility index (%) for superdisintigant and the entire formulation blend ranged from 12.47667±0.365559% to 15.00667±0.339755%. and 12.90±2.985 to 14.52±1.25.

3.3 Post Compression Studies

A) Hardness:

The hardness of all the tablets prepared by both methods was maintained within the 3.156667±0.040415 kg/cm^2 to 3.356667±0.040415 kg/cm^2. The mean hardness test results are tabulated in Table 5.

B) Friability test:

The friability was found in all designed formulations in the range 0.506667±0.025166 to 0.746667±0.025019 to be well within the approved range (< 1 %) .The friability study results were tabulated in Table 5.

C) Weight variation test:

The weight variation was found in all designed formulations in the range 150.128±0.405941 to 150.379±0.459528 mg. The mean weight variation test results are tabulated in Table 6.

D) Thickness:

The mean thickness was (n=3) almost uniform in all the formulations and values ranged from3.3033±0.04509 mm to 3.476±0.05116 mm. The results of thickness for tablets were shown in Table 5.

E) *In vitro* dispersion time:

The *in vitro* dispersion time is measured by the time taken to undergo uniform dispersion. Rapid dispersion within several minutes was observed in all the formulations. The *in-vitro* dispersion data is tabulated in the Table 5.

F) Wetting time:

The results of wetting time are shown in Table 6. The wetting time of Amlodipine besylate prepared by direct compression was found to be in the range of 29.91-69.1 sec. Promising formulations CP5 and PM5showed a wetting time of 29.91667±1.52752530 and 40.59±0.675056 sec respectively, which facilitate the faster dispersion.

Table 5. Evaluation of Amlodipin Besylate FDT Formulations [1]

Formulation code	Parameters			
	Hardness (kg/cm^2)	Friability (%)	Thickness (mm)	*In vitro* Dispersion time (sec)
CP0	3.2±0.05	0.7367±0.01575	3.36±0.12165	105.1633±0.575 29
PM1	3.2033±0.04592	0.6367±0.0107	3.3567±0.0815	60.0667± 0.5991
PM2	3.1967±0.0452	0.593±0.01262	3.43±0.05	62.84±0.60108 2
PM3	3.1567±0.0415	0.627±0.00839	3.476±0.0516	64.2467±1. 186816
PM4	3.253±0.04509	0.7167±0.0114	3.2833±0.02081	59.86333 ±0.37018
PM5	3.25±0.05	0.7467±0.0250	3.3833±0.02081	49.9867±0.43 6501
CP1	3.3567±0.0404	0.6267±0.0251	3.4566±0.04045	55.16±0. 282135
CP2	3.2967±0.0550	0.6167±0.0208	3.3033±0.05686	61.9467± 0.535288
CP3	3.35±0.05	0.5467±0.0152	3.3033±0.04509	57.2133±0.30 0888
CP4	3.2267±0.0321	0.5067±0.0251	3.46±0.04	45.357±4.2350 72
CP5	3.3067±0.0513	0.523±0.02516	3.433±0.0416	38.773±1.3 47825

Table 6. Evaluation of amlodipin besylate FDT formulations [2]

Formulation code	Parameter			
	Wetting time (sec)	Water absorption Ratio (%)	Percent drug content	Weight Variation
CP 0	69.1±31.26927	51.95±1.571623	97.623±0.58192	150.28± 0.473357
PM1	50.7967±0.5034	44.357±1.02342	98.88±0.612726	150.18 ±0.440954
PM2	58.7167±0.5181	48.337±0.67532	100.4±0.632376	150.238±0.44757
PM3	54.72±0.475079	57.167±0.94495	98.773±0.29023	150.12 8±0.40594
PM4	50.893±0.32036	63.863±0.49034	99.3067±0.1724	150.18 9±0.47125
PM5	40.59±0.675056	71.423±1.15697	100.217±0.4054	150.13 5±0.48653
CP1	48.48±1.154426	52.437±1.07062	98.5±0.326599	150.168 ±0.44329
CP2	51.27±1.080139	55.283±0.940443	97.01±0.420555	150.292±0.4361
CP3	44.29±1.087796	64.45±0.72111	96.79±0.379737	150.239 ±0.4188
CP4	40.35±0.934077	73.3767±0.95318	98.633±0.236291	150.19±0.48651
CP5	29.9167±1.52755	76.6367±1.5847	99.663±0.14019	150.379±0.45958

G) Water absorption ratio:

The values of water absorption ratio shown in Table 6. water absorption ratio was found to be in the range of 44.357±1.02342 to 76.6367±1.5847.PM5 and CP5 formulations shows 71.423±1.15697 and 76.6367±1.5847 respectively.

H) Drug Content:

The drug content uniformity was performed for all the 11 formulations and results are tabulated in Table 6. Three trials from each batch were analyzed spectrophotometrically. The average value and standard deviations of all the formulations were calculated. Drug content in tablet was found to be in the range 96.79±0.379737 to 100.4±0.632376.

3.4 Dissolution Study

Dissolution study of amlodipine besylate was carried out in phosphate buffer 6.8 pH. The % drug release of all the formulations were presented in Fig. 4.

The results of dissolution studies of formulations CP0 is composed of without superdisintigrant and the release profile is given in Fig. 4. It shows minimum drug release because of absence of superdisintigrant. It shows only 75.375±1.12 % drug release. (Table 7). The formulation CP1 CP2 CP3 CP4 CP5 containing co-processed superdisintigrant in various ratio of crosspovidone and sodium starch glycolate (1:1, 1:2, 1:3, 2:1, 3:1). The formulation CP5 shows 98.25±0.35 % drug release in 20 min.due to the porous nature of superdisintigrant.(Table 8). Porous nature is due to the use of solvent evaporation method. As the concentration of crospovidone increases the rapid disintegration and drug release from tablet takes place.

In the formulation PM1, PM2, PM3, PM4, PM5 containing same proportion of superdisintigrant that of co-processed mixture. The physical mixtures prepared without use of solvent.they are directly mixed together. Physical mixture formulations PM5 (3:1) batch shows 97.62±0.835 % drug release at 20 min shows in Fig. 4 the drug release is lower than that of co-processed formulation because of absence of porous nature.

Table 7. In vitro cumulative release of Amlodipine besylate (physical mixture)

Time	% Drug release					
	CP0	PM 1	PM 2	PM 3	PM 4	PM 5
0	**0**	0	0	0	0	0
1	14.26±0.67	40.12±1.357	48.12±1.12	41.28±1.09	45.66± 0.95	55.23±0.87
2	30.54±1.05	45.52±1.71	55.41±1.27	47.26±1.075	49.4±1 .07	62.25±0.96
3	35.69±0.82	51.4±0.91	61.24±1.07	53.36±0.6	55.46±0.9 1	69.85±0.94
4	41.746±1.71	60.6±1.71	65.36±1.17	63.40±1.02	65.45±1 .30	73.44±1.01
5	46.53±1.26	62.9±1.45	68.24±1.42	65.54±0.55	68.378±0 .776	78.896±1.51
10	55.65±1.52	71.42±1.34	70.62±1.40	75.32±1.066	79.65± 0.92	85.536±0.917
15	62.325±0.925	80.56±1.60	81.96±1.16	83.42±1.01	85.35 ±1.16	90.236±1.45
20	75.375±1.12	90.45±1.51	91.45±0.92	95.72±0.425	96.45 ±0.94	97.62±0.835

Table 8. In vitro cumulative release of Amlodipine besylate(co-processed mixture)

Time	% Drug release				
	CP 1	CP 2	CP 3	CP 4	CP 5
0	0	0	0	0	0
1	45.45±0.98	51.516±1.10	55.465±1.03	55.523±0.902	62. 24±1.01
2	48.56±1.09	55.59±1.32	56.45±0.82	60.46±0.95	67.199± 1.47
3	55.53±1.082	63.469±0.867	61.62±1.14	65.325±1.07	71. 756±1.54
4	63.46±0.78	67.32±0.78	65.39±1.01	71.32±1.08	74.62±1 .15
5	65.84±0.96	71.52±1.04	72.48±1.16	75.61±1.06	80.31±1 .11
10	75.26±0.951	77.52±1.02	77.66±0.94	81.35±0.94	90.33± 1.23
15	83.813±1.18	85.42±1.29	85.83±1.36	91.83±1.755	95.97 5±
20	90.16±1.456	92.55±1.13	94.95±1.3	95.281±1.10	98.25± 0.35

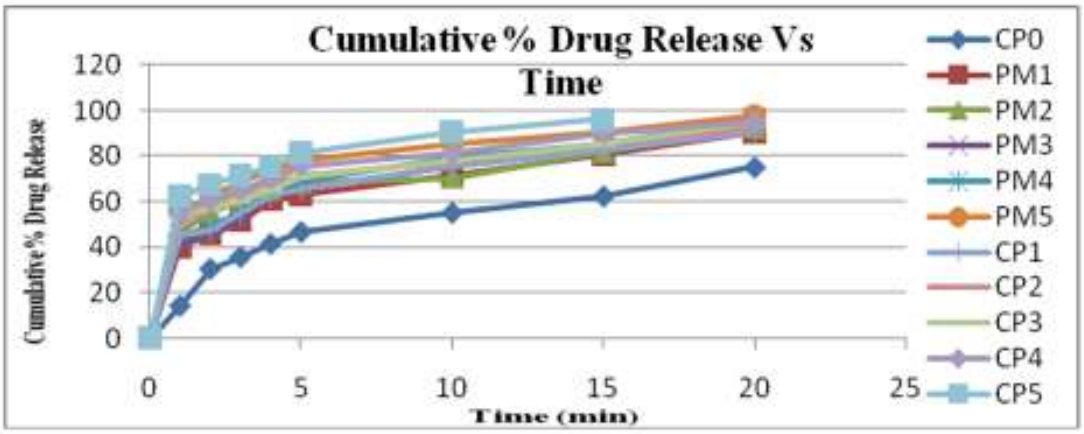

Fig. 4. in vitro cumulative drug release of amlodipne besylate batches from CP0 - CP5
(Each point represents mean ± SD, n=3)

3.5 Result of Stability Study

The promising formulations were subjected to short term stability study by storing at 40ºC/75%RH for one month. The formulations PM1, PM5, CP1, and CP5 were selected. After one month tablets were analyzed for hardness friability dispersion time % drug release. There is no changes in the result of tablets (Table 9).

Table 9. Result of stability study

Sr. no.	Formulation code	Hardness	Friability	Dispersion time	% drug release
1	**PM1**	3.3033±0.04592	0.667±0.0107	62.0667±0.5991	88.45±1.51
2	**PM5**	3.45±0.05	0.767±0.0250	51.9867±0.436501	95.62±0.835
3	**CP1**	3.5567±0.0404	0.6567±0.0251	56.16±0.282135	89.16±1.456
4	**CP5**	3.4067±0.0513	0.543±0.02516	41.773±1.347825	96.25±0.35

4. CONCLUSION

The use of Co-processed superdisintegrants consists of crospovidone and sodium starch glycolate in formulation exhibit good flow and compression characteristics. Amlodipin Besylate tablets containing co-processed superdisintegrants exhibit quick disintegration and improved drug dissolution. It can be concluded from the present work that co-processed superdisintegrants of crospovidone and sodium starch glycolate are superior to physical mixtures of crospovidone and sodium starch glycolate used in Amlodipin Besylate fast dissolving tablets.

CONSENT

Not applicable.

ETHICAL APPROVAL

Not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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