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FORMULATION, DEVELOPMENT AND EVALUATION OF FAST DISINTEREATING COMBINATION AMLODIPIN BESYLATE AND ATENOLOL TABLET USING NATURAL DISINTIGRANT

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ABSTRACT

The present study aimed to develop fast disintegrating tablets of Amlodipine besylate and Atenolol using natural disintegrants like Guar gum, Gum Karaya & synthetic super disintegrants like Croscaramellose sodium, Sodium starch glycolate and crospovidone. Disintigrant concentration was taken in this studies 1%, 2%, 3%. Precompressional studies revealed good micromeritic properties of powder blend. Various Formulations of were prepared by direct compression method and were evaluated for their physico chemical properties, drug release and stability studies The hardness, friability, drug content and disintegration time of fast dissolving tablets were found uniform and reproducible. Dissolution test shows that 3 % w/w concentration was found optimum for both disintigrant. Optimized formulation was compare with marketed formulation. Drug release of marketed formulation was only 97.65% AML 98.91% ATEN at the end of 24 min which is much less as compared to the optimized batch (F_3 & F_6) which showed drug release of 101.75% AML 100.52% ATE for F3 batch and 99.92% AML 100.51% ATEN for F6 batch at the end of 18 min.

KEYWORDS: Guar gum, Gum karaya, natural disintegrant, Fast disintegrant tablet.

INTRODUCTION

Fast disintegrating tablets are also called as mouth-dissolving tablets, melt-in mouth tablets, Orodispersible tablets, rapid melts, porous tablets, quick dissolving etc. Fast disintegrating tablets are those when put on tongue disintegrate instantaneously releasing the drug which

dissolve or disperses in the saliva. The faster the drug into solution, quicker the absorption and onset of clinical effect. Some drugs are absorbed from the mouth, pharynx and esophagus as the saliva passes down into the stomach. In such cases, bioavailability of drug is significantly greater than those observed from conventional tablets dosage form.[1] Chemically Atenolol is 4-(2-Hydroxy-3-[(1-methyl ethyl) amino] propoxy) benzene acetamide[2] ß1-blocker is prescribed widely in diverse cardiovascular diseases, eg, hypertension, angina pectoris, arrhythmias, and myocardial infarction. The drug is also frequently indicated in the prophylactic treatment of migraine.[3] Oral bioavailability of Atenolol is around 50% and having half life 6 to 7 hrs.[4] Amlodipine belongs to a class of medications called calcium channel blockers. These medications block the transport of calcium into the smooth muscle cells lining the coronary arteries and other arteries of the body. Since calcium is important in muscle contraction, blocking calcium transport relaxes artery muscles and dilates coronary arteries and other arteries of the body. By relaxing coronary arteries, amlodipine is useful in preventing chest pain (angina) resulting from coronary artery spasm. Relaxing the muscles lining the arteries of the rest of the body lowers the blood pressure, which reduces the burden on the heart as it pumps blood to the body. Reducing heart burden lessens the heart muscle's demand for oxygen, and further helps to prevent angina in patients with coronary artery disease. The usual initial antihypertensive oral dose of Amlodipine besylate tablets is 5 mg once daily with a maximum dose of 10 mg once daily.[5-6] Another prerequisite for the fast dissolution may be the disintegration time of tablets because; faster disintegration of tablets delivers a fine suspension of drug particles and thus, greater dissolution of the drug.[7] Solid oral dosage forms, especially tablets, remain one of the most popular because of advantages like patient convenience, ease of storage and dispensing, dose accuracy and easy manufacturability. Solid oral dosage forms, especially tablets, remain one of the most popular because of advantages like patient convenience, ease of storage and dispensing, dose accuracy and easy manufacturability

MATERIAL AND METHOD

Chemical and Drugs

Atenolol was procured as a gift sample from Hetro drug Ltd., Amlodipine besylate was procured as a gift sample from Inland Pharma Ltd. Croscarmellose sodium, Crospovidone, directly compressible. Microcrystalline cellulose PH102 were procured as a gift sample from Ankit Pulps and Boards Pvt. Ltd., Magnesium sterate was procured as a gift sample from Likir

Chemicals Pvt. Ltd, Colloidal silicon dioxide was procured as a gift sample from Likir Chemicals Pvt. Ltd. and all other chemicals and reagents used were Analytical grade.

Preparation of fast disintegrating tablets

Fast disintegrating tablets of atenolol and Amlodipine were prepared by direct compression method formula for tablet preparation is shown in Table 1-2 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 300 mg using 8.5mm concave flat punches on 12-station Karnavati Mini press-II tablet machine.

TABLE 1: Formulation of Amlodipine & Atenolol by Direct Compression Method

Sr.No.	Ingredients	Formulation Code (Qty/tab. In mg)							
		F1	F2	F3	F4	F5	F6	F7	F8
1	Amlodipine Besylate	5.41	5.41	5.41	5.41	5.41	5.41	5.41	5.41
2	Atenolol	50.00	50.00	50.00	50.00	50.00	50.00	50.00	50.00
3	Microcrystalline Cellulose	50.00	50.00	50.00	50.00	50.00	50.00	50.00	50.00
4	Maize Starch	180.10	177.10	174.10	180.10	177.10	174.10	180.10	177.10
5	Colloidal Silicon Dioxide	6.00	6.00	6.00	6.00	6.00	6.00	6.00	6.00
6	PVP K-30	2.00	2.00	2.00	2.00	2.00	2.00	2.00	2.00
7	Aspartame	1.49	1.49	1.49	1.49	1.49	1.49	1.49	1.49
8	Guar gum	3.00	6.00	9.00	….	….	….	….	….
9	Gum Karaya	….	….	….	3.00	6.00	9.00	….	….
10	Crossprovidone	….	….	…..	…	…	…..	3.00	6.00
11	Sodium Starch Glycolate	….	….	….	….	….	….	….	….
12	Croscarmellose Sodium	….	….	….	….	….	….	….	….
13	Magnesium Stearate	2.00	2.00	2.00	2.00	2.00	2.00	2.00	2.00
	Total weight of Tablet	300	300	300	300	300	300	300	300

TABLE 2: Formulation of Amlodipine & Atenolol by Direct Compression Method

Sr. No.	Ingredients	Formulation Code (Qty/tab. In mg)						
		F9	F10	F11	F12	F13	F14	F15
1	Amlodipine Besylate	5.41	5.41	5.41	5.41	5.41	5.41	5.41
2	Atenolol	50.00	50.00	50.00	50.00	50.00	50.00	50.00
3	Microcrystalline Cellulose	50.00	50.00	50.00	50.00	50.00	50.00	50.00
4	Maize Starch	174.10	180.10	177.10	174.10	180.10	177.10	174.10
5	Colloidal Silicon Dioxide	6.00	6.00	6.00	6.00	6.00	6.00	6.00
6	PVP K-30	2.00	2.00	2.00	2.00	2.00	2.00	2.00
7	Aspartame	1.49	1.49	1.49	1.49	1.49	1.49	1.49
8	Guar gum	….	….	….	….	….	….	….

9	Gum Karaya	….	….	….	….	….	….	….
10	Crossprovidone	9.00	….	….	….	….	….	…
11	Sodium Starch Glycolate	….	3.00	6.00	9.00	….	….	….
12	Croscarmellose Sodium	….	….	….	….	3.00	6.00	9.00
	Magnesium Stearate	2.00	2.00	2.00	2.00	2.00	2.00	2.00
	Total weight of Tablet	300	300	300	300	300	300	300

Evaluation

Preparation of calibration curve of Amlodipine besylate and Atenolol in phosphate buffer (pH 6.8)

(i) Preparation of standard stock solution: About 10 mg of Amlodipine besylate was first dissolved in 10 mL of phosphate buffer (pH 6.8). Approximately 10 mL of this solution was then transferred to a 100 mL volumetric flask. The volume of solution was made up by using the phosphate buffer (pH 6.8) to give a solution of concentration 100 µg/mL.Table 3.

(ii) Preparation of standard stock solution: About 10 mg of Atenolol was first dissolved in 10 mL of phosphate buffer (pH 6.8). Approximately 10 mL of this solution was then transferred to a 100 mL volumetric flask. The volume of solution was made up by using the phosphate buffer (pH 6.8) to give a solution of concentration 100 µg/Ml. Table 4

TABLE 3: ATENOLOL

Sr.No.	Concentration in µg/ml	Absorbance at 238nm
1	2	0.2183
2	4	0.3424
3	6	0.5636
4	8	0.6855
5	10	0.8053

TABLE 4: AMLODIPINE

Sr. No.	Concentration (µg/mL)	Absorbance at 224 nm
1.	2	0.0901
2.	4	0.1572
3.	6	0.2295
4.	8	0.3097
5.	10	0.3713

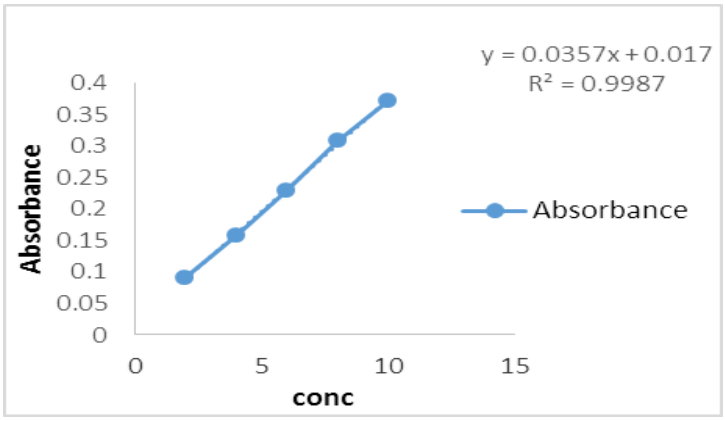


Fig 1: Standard Calibration Curve of Atenolol by using pH 6.8 Phosphate Buffer

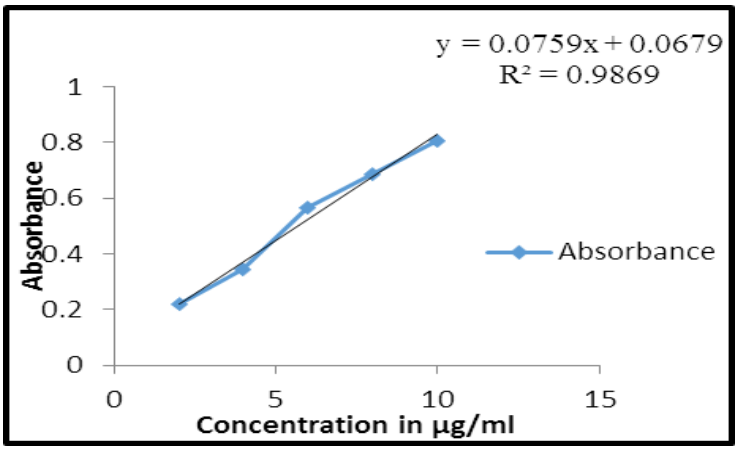


Fig 2: Standard Calibration Curve of Amlodipine besylate by using pH 6.8 Phosphate Buffer

Pre-compretion evaluation

Angle of repose: Flow ability of blend was determined by calculating angle of repose by fixed height method. A funnel with 10 mm inner diameter of stem was fixed at a height of 2 cm. over the platform. About 10 gm of sample was slowly passed along the wall of the funnel. A rough circle was drawn around the pile base and the radius of the powder cone was measured. Angle of repose was calculated from the average radius using the following formula:

$$\tan \theta = h/r \qquad \text{OR}$$

$$\theta = \tan^{-1} h/r$$

where, θ is the angle of repose, h is the height of the conical pile and r is the radius of the conical pile.[8]

Bulk density: Bulk density was determined by pouring gently 10 gm of sample through a glass funnel in to a 100 mL graduated cylinder. The volume occupied by the sample was recorded. Bulk density was calculated.[8]

$$\text{Bulk density } (\rho_0) = \frac{M}{V_0}$$

Where, ρ_0 = Bulk density

M = Mass of powder taken

V_0 = Apparent unsettled volume

Tapped density: 10 gms sample (tablet blend) was poured gently through a glass funnel in to a 100mL graduated cylinder. The cylinder was tapped from height of 2 inches until a constant volume was obtained. Volume occupied by the sample after tapping were recorded and tapped density was calculated.[8]

$$\text{Tapped density } (\rho_0) = \frac{M}{V_t}$$

Where, ρ_t = tapped density

M = weight of powder

V_t = tapped volume of powder in cm^3

Hausner's ratio: Hausner ratio is an indirect index of ease of powder flow. It is calculated by the following formula,

$$\text{Hausner's ratio} = \frac{\rho_t}{\rho_0}$$

Lower Hausner's ratio = better flow ability

Higher Hausner's ratio = poor flow ability.[9,10]

Compressibility index: Tapped and bulk density measurements can be used to estimate the Carr's index of a material. Carr's index was determined by,[11]

$$C = \frac{\rho_t - \rho_0}{\rho_t} \times 100$$

Where, ρ_t = Tapped density

ρ_0 = Bulk density

C = Compressibility index

Post-compression parameter (physical parameters)

Thickness: The thickness of the tablets was determined using a Dial caliper (Advance). Three tablets from each type of formulation were used and average values were calculated. It is expressed in mm.[12]

Hardness: The resistance of tablets to shipping, breakage, under conditions of storage, transportation and handling before usage depends on its hardness. For each formulation, the hardness of 6 tablets was determined using the Monsanto hardness tester. The tablet was held along its diametrical axis in between the two jaws of the tester. At this point, reading should be zero kg/cm^2. Then constant force was applied by rotating the knob until the tablet fractured. The value at this point was noted.

Friability: Friability is the measure of tablet strength. Roche Friabilator was used for testing the friability using the following procedure. This test subjects a number of tablets to the combined effect of shock abrasion by utilizing a plastic chamber which revolves at a speed of 25 rpm, dropping the tablets to a distance of 6 inches in each revolution. A sample of pre-weighed 10 tablets was placed in Roche friabilator which was then operated for 100 revolutions i.e. 4 minutes. The tablets were then dusted and reweighed. A loss of less than 1 % in weight in generally considered acceptable[8] Percent friability (% F) was calculated as follows

$$\% \text{ Friability} = \frac{\text{Initial weight-final weight}}{\text{Initial weight}} \times 100$$

Weight variation test: To find out weight variation, 20 tablets of each type of formulation were weighed individually using an electronic balance, average weight was calculated and individual tablet weight was then compared with average value to find the deviation in weight.[8]

Disintegration time: The disintegration time for fast Disintigranting tablet was measured using the conventional test for tablets as described in the Pharmacopoeia. Tablets were placed in the disintegration tubes and time required for complete disintegration without leaving any residues on the screen was recorded as disintegration time.[12]

Wetting time: Wetting time corresponds to the time taken for the tablet to disintegrate when kept motionless on the tongue. Wetting time is closely related to the inner structure of the

tablets and to the hydrophilicity of the excipient. A piece of tissue paper folded double was placed in a petri plate (internal diameter is 10 cm) containing 6 ml of water. The tablet was placed on the paper and the time for complete wetting of the tablet was measured in seconds. The method was slightly modified by maintaining water at 37 ˚C.[13]

Water absorption ratio: The weight of the tablet prior to placement in the petridish was noted (Wb) using digital balance (Shimadzu, Japan). The wetted tablet was removed and reweighed (Wa). Water absorption ratio (R), was then calculated according to the following equation.[14]

$$R = \frac{Wa - Wb}{Wb} \times 100$$

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

Evaluation of pre-compression parameters

Evaluation of powder blend: The prepared powder mixtures were evaluated for the blend property like bulk density, tapped density, Carr's index, angle of repose and Hausner's ratio. Results obtained are given in **TABLE 5-6.**

TABLE 5

Formulation Code	Evaluation parameters				
	Bulk density (g/cc)	Tapped density (g/cc)	Angle of repose (θ)	Carr's Index (%)	Hausner's Ratio
F1	0.4692	0.544	31.79	21.24	1.1594
F2	0.4421	0.532	30.24	16.89	1.2033
F3	0.4536	0.549	28.3	21.02	1.2130
F4	0.4612	0.561	30.1	21.35	1.2163
F5	0.4432	0.531	31.32	16.53	1.1981
F6	0.4476	0.536	32.11	16.49	1.1974
F7	0.4592	0.562	30.02	18.29	1.2238
F8	0.4416	0.551	28.90	19.85	1.2477

TABLE 6

Formulation Code	Evaluation parameters				
	Bulk density (g/cc)	Tapped density (g/cc)	Angle of repose (θ)	Carr's Index (%)	Hausner's Ratio
F9	0.440	0.542	29.10	18.80	1.2315
F10	0.470	0.554	28.41	21.91	1.1787
F11	0.458	0.545	31.79	22	1.1899
F12	0.442	0.531	28.67	16.76	1.2013
F13	0.471	0.559	30.16	24.68	1.1868
F14	0.485	0.580	28.37	27.10	1.1958
F15	0.447	0.543	30.11	17.79	1.2147

Evaluation of fast disintigeating tablets (post compression parameters) table 7-8.

TABLE 7

Physical parameters of Fast disintegrating tablets

Formulation Code	Weight variation(mg)	Hardness(kg/cm^2)	Thickness(mm)	Friability test(%)
F1	299.60±3.31	2.93±0.11	3.32±0.02	0.219±0.18
F2	299.60±2.41	3.03±0.05	3.34±0.02	0.261±0.10
F3	300.00±1.74	3.36±0.15	3.39±0.08	0.183±0.01
F4	299.45±3.70	3.33±0.28	3.41±0.02	0.311±0.10
F5	299.85±4.19	3.03±0.05	3.35±0.06	0.337±0.03
F6	300.1±2.46	2.8±0.26	3.37±0.03	0.468±0.36
F7	299.85±3.61	3.1±0.36	3.35±0.04	0.581±0.34
F8	300.4±3.47	3.0±0.0	3.35±0.04	0.493±0.34

(*mean of three values ± SD)

TABLE 8

Formulation Code	Weight variation(mg)	Hardness(kg/cm^2)	Thickness(mm)	Friability test(%)
F9	299.95±2.72	3.03±0.05	3.33±0.03	0.581±0.30
F10	299.2±3.12	3.16±0.28	3.37±0.01	0.493±0.36
F11	300.2±2.46	3.06±0.11	3.33±0.03	0.581±0.20
F12	299.9±2.51	3.26±0.23	3.32±0.03	0.458±0.06
F13	300.1±3.49	3.00±0.0	3.36±0.01	0.583±0.15
F14	299.85±2.36	3.1±0.10	3.33±0.03	0.139±0.10
F15	299.75±2.29	3.16±0.28	3.32±0.005	0.217±0.27

(*mean of three values ± SD)

Results of disintegration time, wetting time and water absorption ratio of fast disintigrating tablets (table 9-10)

TABLE 9

Formulation Code	Disintegration time(sec)	Wetting time (Sec)	Water absorption ratio
F1	17.33±1.24	8.44±0.23	75.83±1.21
F2	18.33±0.47	8.12±0.15	93.26±0.43
F3	14.00±0.81	6.43±0.13	101.01±2.12
F4	21.33±0.47	8.25±0.07	79.39±1.83
F5	17.33±0.47	8.23±0.028	93.00±1.53
F6	14.66±0.47	7.13±0.04	99.33±0.78
F7	16.33±0.47	7.07±0.47	65.44±2.51
F8	16.00±0.81	9.31±0.51	74.91±1.73

(*mean of three values ± SD)

TABLE 10

Formulation Code	Disintegration time(sec)	Wetting time (Sec)	Water absorption ratio
F9	15.66±0.47	7.25±0.11	89.43±2.54
F10	15.00±0.81	9.37±0.05	87.62±2.10
F11	14.33±0.47	8.82±0.10	98.67±0.24
F12	14.66±0.94	7.19±0.04	76.84±0.84
F13	19.66±1.24	8.03±0.10	73.24±0.71
F14	16.66±0.47	7.86±0.08	80.06±1.96
F15	17.33±0.94	9.39±0.08	87.91±2.11

Chemical parameters

Uniformity of drug content: The test for uniformity of content of single dose preparation is based on the assay of individual content of active substance(s) of a number of single dose units to determine whether the individual contents are within limits set with reference to the average content[12] (TABLE 11).

Results of uniformity of content of fast disintegrating tablets. (table 11)

TABLE 11

Parameters →	**Uniformity of content***	
Batches ↓	AML	ATE
F1	98.54±0.70	98.31±0.28
F2	97.65±0.026	100±0.56
F3	99.82±0.66	100.46±0.70
F4	96.11±0.02	100.18±0.58
F5	98.76±0.015	98.69±0.42
F6	99.02±0.02	100.56±1.22
F7	96.51±0.15	99.53±0.42
F8	98.26±0.29	100.28±1.74
F9	96.77±0.046	99.25±0.85
F10	98.12±0.027	100.18±0.42
F11	99.29±0.06	100.74±1.06
F12	95.66±0.15	98.69±0.70
F13	96.66±0.04	98.78±0.58
F14	96.10±0.020	97.81±0.05
F15	96.57±0.24	96.90±0.75

Dissolution studies: The *in-vitro* drug release was determined using USP dissolution testing apparatus type-II (paddle type). The dissolution test was performed using 900 mL of phosphate buffer (pH 6.8), at 37 ºC ± 0.5 ˚C and 50 rpm. Sample volume of 10 mL was withdrawn at regular time intervals of 3, 6, 9, 12,15,18 min. from a zone midway between the surface of dissolution medium and the top of rotating paddle not less than 1 cm apart from the vessel wall. The volume withdrawn was replaced by fresh volume of dissolution medium to maintain constant volume of medium. The filtered samples were analyzed spectrophotometrically at 238nm and 224nm using phosphate buffer (pH 6.8) as a blank.[15]

TABLE 12

Percentage cumulative drug release of F1 to F6 batches (AML)

Time (in min)	**F1**	**F2**	**F3**	**F4**	**F5**
3	66.00±1.73	69.58±2.19	82.86±1.71	69.05±2.00	75.33±1.13
6	69.821±1.37	73.35±1.60	88.07±2.63	75.09±1.13	79.01±0.48
9	77.32±1.12	80.12±0.50	90.38±1.81	79.29±0.35	82.723±0.74
12	82.62±1.01	86.52±2.23	94.17±0.77	87.60±0.92	88.40±1.56
15	89.08±3.20	93.24±1.40	98.05±0.28	91.08±1.95	92.48±1.14
18	96.96±1.26	98.26±0.74	101.75±1.60	93.81±1.26	97.63±1.02

TABLE 13

Percentage cumulative drug release of F6 to F10 batches (AML)

Time (in min)	F6	F7	F8	F9	F10
3	79.25±1.09	70.31±2.03	79.70±0.12	72.69±0.43	82.55±1.66
6	82.84±1.39	72.88±4.37	82.12±0.50	77.07±0.91	86.48±2.33
9	86.47±1.03	80.69±0.86	84.05±0.09	80.07±0.52	89.75±1.62
12	89.86±0.56	86.36±0.28	87.1±0.17	83.72±0.17	93.12±1.54
15	95.25±0.89	90.97±0.41	94.51±1.25	89.52±0.43	95.68±1.04
18	99.92±0.23	94.39±0.54	96.84±0.89	97.03±0.43	97.47±1.30

TABLE 14

Percentage cumulative drug release of F11 to F15 batches (AML)

Time (in min)	F11	F12	F13	F14	F15
3	83.83±0.71	77.07±1.18	69.39±0.68	72.80±1.00	71.68±0.63
6	88.85±0.13	80.94±2.70	76.78±1.00	76.71±0.88	74.93±0.79
9	91.33±0.66	85.58±2.55	80.62±0.15	82.64±0.45	78.38±0.23
12	93.95±0.39	91.42±1.91	82.46±1.02	87.64±0.94	82.12±0.14
15	96.75±0.50	95.27±1.08	90.36±0.80	94.73±0.74	88.9±0.46
18	99.02±0.64	97.39±0.42	93.73±0.90	97.52±0.56	96.88±0.21

TABLE 15

Percentage cumulative drug release of F1 to F5 batches (ATEN)

Time (in min)	F1	F2	F3	F4	F5
3	80.47±0.86	79.22±1.41	89.36±0.99	82.15±1.62	84.11±0.90
6	82.72±1.49	82.66±1.29	92.10±0.58	83.91±2.66	86.71±0.84
9	86.63±1.22	86.45±0.37	94.40±0.05	87.06±2.76	90.31±0.76
12	89.45±1.05	89.12±1.42	96.99±0.54	90.88±1.54	92.00±0.21
15	93.75±0.29	92.35±0.65	99.25±0.35	93.34±1.01	93.45±0.035
18	96.13±0.75	94.45±0.42	100.52±1.52	95.96±0.13	96.30±0.46

TABLE 16

Percentage cumulative drug release of F6 to F10 batches (ATEN)

Time (in min)	F6	F7	F8	F9	F10
3	88.00±0.92	83.02±0.86	82.82±1.26	87.14±1.53	83.19±1.26
6	90.39±0.62	85.54±1.14	85.69±0.41	89.11±0.87	87.43±2.27
9	92.77±0.04	88.68±1.24	87.54±0.57	90.71±0.64	90.29±2.35
12	94.44±0.26	91.52±0.87	90.27±0.23	92.45±0.51	91.89±1.80
15	98.01±0.53	94.66±0.64	92.61±0.62	94.43±0.52	95.44±0.84
18	100.51±0.04	98.20±0.60	94.42±0.48	97.89±0.36	97.17±0.74

TABLE 17

Percentage cumulative drug release of F11 to F15 batches (ATEN)

Time (in min)	F11	F12	F13	F14	F15
3	82.62±1.77	83.80±1.05	80.38±0.42	81.45±0.84	81.22±1.33
6	87.02±2.05	85.73±1.40	82.90±0.66	83.74±1.39	83.72±1.33
9	89.79±1.65	88.69±1.16	85.04±1.12	86.17±1.45	86.01±0.75
12	94.69±1.12	91.82±1.04	88.56±1.34	89.15±1.65	88.75±0.37
15	97.24±0.60	95.62±0.81	91.92±0.28	92.86±0.81	91.63±0.73
18	99.65±0.25	98.04±0.30	94.08±0.31	96.60±0.51	95.70±0.28

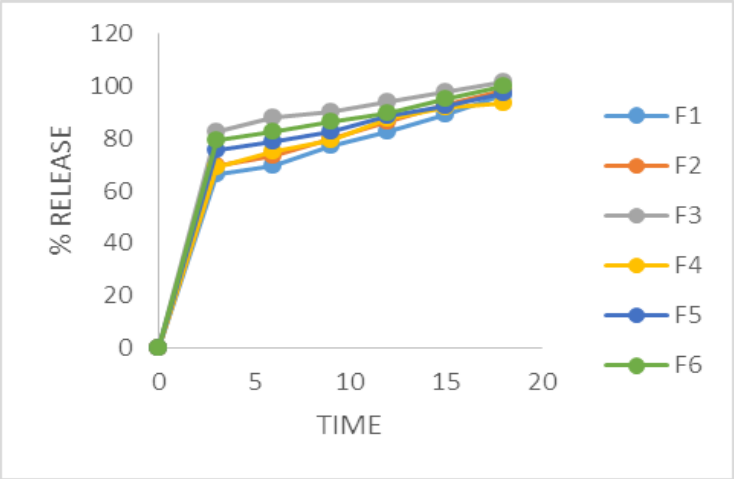


Fig. 3 Graphical presentation of comparative dissolution profile of F1 to F6 formulations (AML)

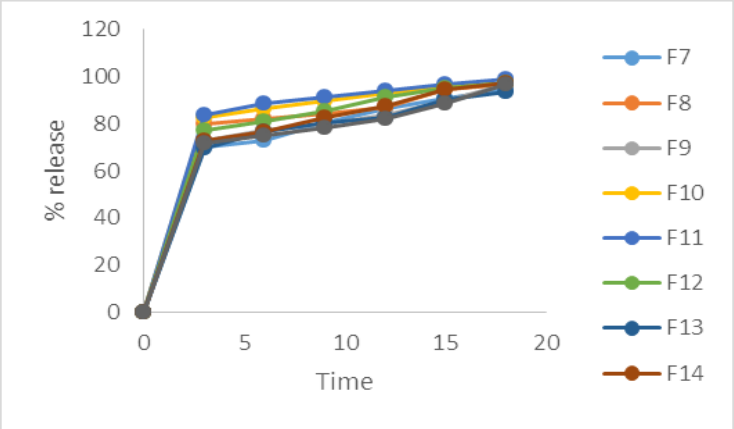


Fig.4 Graphical presentation of comparative dissolution profile of F7 to F15 formulations (AML)

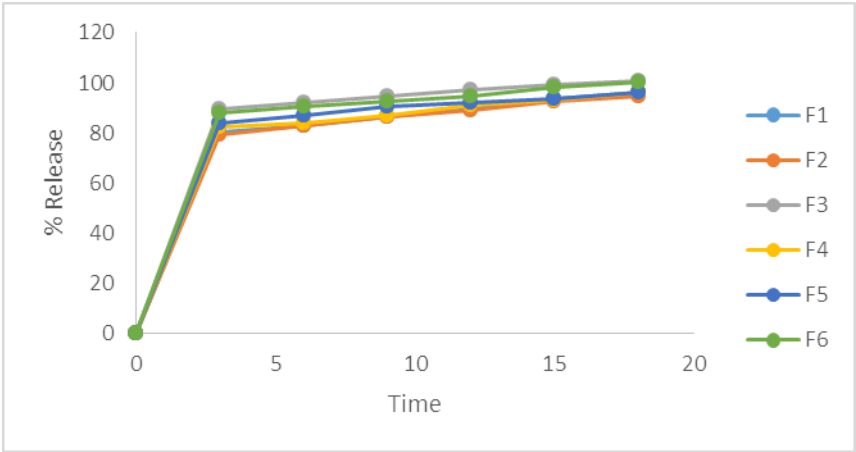


Fig. 5 Graphical presentation of comparative, dissolution profile of F1 to F6 formulations (ATEN)

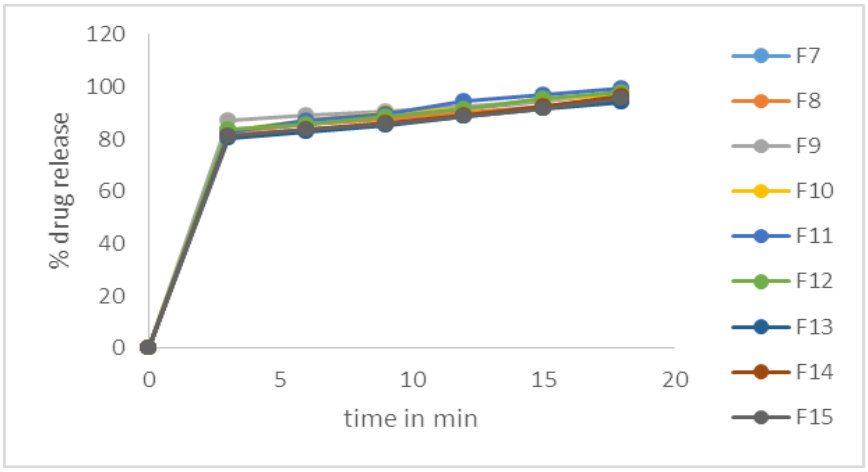


Fig.6.Graphical presentation of comparative dissolution profile F7 To F15 formulation(ATEN).

Optimizaed formulation

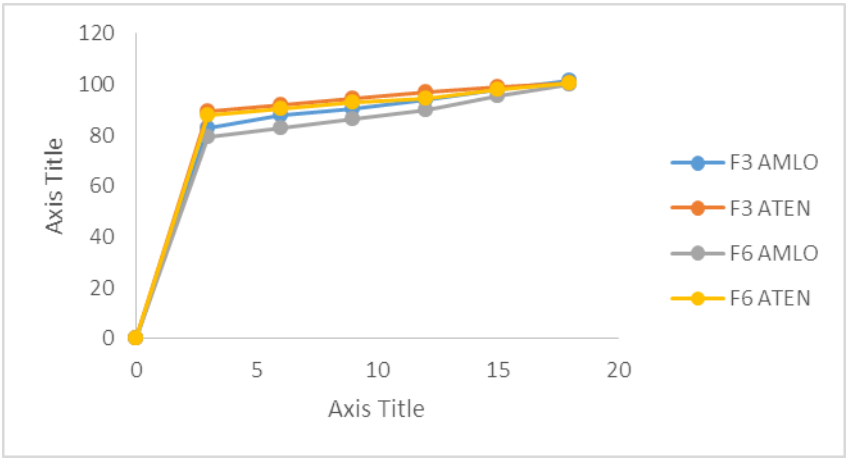


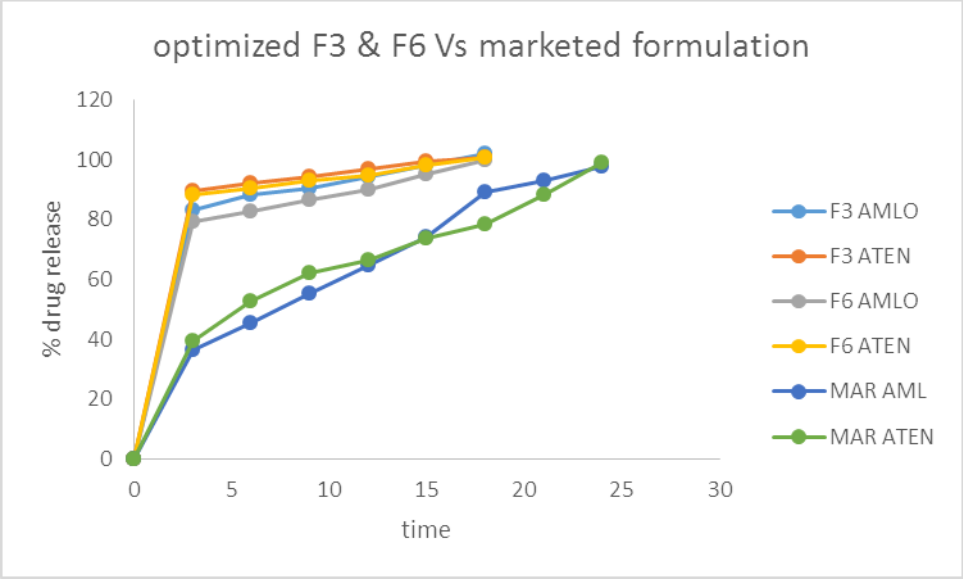
Fig.7.Graphical presentation of optimized bach profile F3 To F6 formulation.

Drug release study of marketed formulation

Marketed formulation of Amlodipin and Atenolol , Amdepin AT. Cadila pharmaceutical Pvt, Ltd. was studied for drug release and it was found that the drug release of marketed formulation was only 97.65% AML 98.91% ATEN at the end of 24 min which is much less as compared to the optimized batch (F_3 & F_6) which showed drug release of 101.75% AML 100.52% ATE for F3 batch and 99.92% AML 100.51% ATEN for F6 batch at the end of 18 min The drug release of marketed tablet, Amdepin AT was shown in TABLE 18**.**

TABLE 18

Time in min	% cumulative drug release					
	F3		F6		MARKETED	
	AML	ATEN	AML	ATEN	AML	ATEN
3	82.86±1.71	89.36±0.99	79.25±1.09	88.00±0.92	36.47±1.84	39.48±0.77
6	88.07±2.63	92.10±0.58	82.84±1.39	90.39±0.62	45.43±3.33	52.79±4.75
9	90.38±1.81	94.40±0.05	86.47±1.03	92.77±0.04	55.20±1.59	62.05±0.71
12	94.17±0.77	96.99±0.54	89.86±0.56	94.44±0.26	64.75±3.34	66.26±0.71
15	98.05±0.28	99.25±0.35	95.25±0.89	98.01±0.53	74.24±3.36	73.67±1.29
18	101.75±1.60	100.52±1.52	99.92±0.23	100.51±0.04	88.86±2.25	78.48±1.26
21	-	-	-	-	93.04±0.92	88.22±0.73
24	-	-	-	-	97.65±1.91	98.91±0.76



RESULT AND DISSCUTION

The Fast Disintegrating tablet that is Amlodipine and Atenolol using natural disintegrant and synthetic superdisintegrant, which was ready for compression, was examined for Angle of repose, Bulk density, Tapped density, Compressibility index, Hausner's ratio and the values for which are as reported in Table no. 5-6. The bulk density of all formulations was found to

be in the range 0.440 to 0.485 gm/ml, whereas the tapped density was observed between 0.531 to 0.580 gm/ml. From the values of bulk density and tapped density the values for Compressibility index and Hausner's ratio were calculated. The values for Compressibility index were found between16.53% to 27.10%. The values for Hausner's ratio were found to be less than 1.25. Angle of repose was found to be less than 30 which indicate good flow of powder. Overall these values indicate good flow properties of powder blend, uniform die fill. Therefore, from this data so obtained, it was decided to go for direct compression of tablets from the powder blends. The weight of all formulations batch tablets was found to be in the range of 299.45 to 300.4. None of the tablet was found to deviate from the average weight of tablets. Hardness test for all formulations was carried out and observations obtained were in the range of be 2.8 to 3.36 kg/cm2. Test for friability was conducted for all formulations, % friability was found to be in the range of 0.13 to 0.58. *In vitro* disintegration time for all formulations was found to be in the range of 14.33 to 21.33sec. whereas the thickness of all formulations containing excipients was found to be uniform as it was obtained in the range of 3.32 to 3.41mm. Drug content of all formulations was observed between 95.66% to 99.82% for Amlodipine besylate and for Atenolol was 97.81 to 100.74% which was within the acceptable Pharmacopoeial limits. All these results were tabulated in Wetting time of tablets are found in the range of 6.43 to 9.39 sec. and the water absorption ratio was found in the range of 65.44±2.5% to 101.01±2.12%. The values for thickness and diameter signify uniformity and it was due to uniformity in die fill, good flow properties, uniform pressure and appropriate punch movement. Drug content for all formulations showed uniformity which indicated that there was an uniform flow and uniform distribution of drug. Weight variation tests for all formulations showed weight variation with deviation less than ±5%, which complies with I.P specification and signifies that there is uniformity in flow of powder blend which leads to uniform die fill. Hardness for all formulations was observed to be proper, which signify that tensile strength of all formulations was maintained after direct compression. Friability test for all formulations indicated that % friability was less than 1%, which complies the I.P specification and reveals that all formulations have possessed good physical strength and can withstand the mechanical shocks that can be observed during handling, shipping and transportation. *In vitro* disintegration study explained that there was decrease in disintegration time with successive increase in concentration of disintegrant in formulations. Wetting time and water absorption ratio was determined for all formulations. Results are shown in Table no.9 and 10. Dissolution rate was studied for all designed formulations. Among the various formulations of fast disintegrating tablet of Amlodipine

besylat and Atenolol, the formulation containing natural disintegrants Guar gum and Gum Karaya in 3% concentration (Batch F3%, F6%) is the best formulation having F3 AML 101.75±1.60, ATEN 100.52±1.52 and F6 AML 99.92±0.23, ATEN 100.51±0.04. drug release in least time and the least time for tablet disintegration. The Dissolution Graph Amlodipine and Atenolol FDT is shown in fig. 3 to Fig6. After that optimized formulation was compare with markted formulation,

CONCLUTION

From the study, it can be concluded that direct compression method showed better disintegration and drug release. The prepared tablets disintegrate within few seconds without need of water, thereby enhancing the absorption leading to its increased bioavailability.

ACKNOWLEDGEMENT

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