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DESIGN AND *IN VIVO* CHARACTERIZATION OF AMLODIPINE BESYLATE ORODISPERSIBLE TABLETS

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ABSTRACT

The present study was intended to develop oral disintegrating tablets of amlodipine besylate (AMD), to give fast relief and also to overcome difficulty in swallowing. Amlodipine fast disintegrating tablets were prepared by using different concentrations (5%, 7.5% and 10%) of superdisintegrants such as sodium starch glycolate (SSG), cross carmalose sodium (CCS), cross povidone (CP), ludiflash, isabgol etc., and were characterized for both pre and post-compression parameters. The drug excipients compatibility study was carried out by using differential scanning calorimetry (DSC) and Fourier transforms infrared spectroscopy (FT-IR) and revealed that there was no possible interaction between them. All the formulations were prepared by direct compression technique and evaluated for their physical characters, *in vitro* drug release and *in vivo* disintegration time. Formulations containing 5% SSG, 5% CP in combination with 5% ludiflash (F16 and F17) showed better dissolution profile and least disintegration time. *In vivo* disintegration time, taste and mouth feel evaluation was conducted for F18 and F19 formulations (n=3).

INTRODUCTION:

Oral route of drug administration have wide acceptance up to 50-60% of total dosage forms. Solid dosage forms are more popular because of ease of administration, accurate dosage, self-medication, pain avoidance and most importantly the patient compliance (Bourne 2002; Vemula and Vera Reddy 2011). The most popular solid dosage forms are tablets and capsules; one important drawback of this dosage forms for some patients especially in geriatrics (Sastry, Nyshadham and Fix 2000), is the difficulty to swallow (dysphagia) (Lindgren and Janzon 1993). Drinking water plays an important role in the swallowing of oral dosage forms. Sometimes people experience inconvenience in swallowing conventional dosage forms such as tablet when water is not available, in the case of the motion sickness (kinetosis) and sudden episodes of coughing during the common cold, allergic condition and bronchitis. For these reasons, tablets that can rapidly dissolve or disintegrate in the oral cavity have attracted a great deal of attention. Orodispersible tablets are not only indicated for people who

have swallowing difficulties, but also are ideal for active people (Seager 1998). Fast dissolving tablets are also called as mouth dissolving tablets, quick disintegrating tablets, melt in mouth tablets, orodispersible tablets, rapimelts, porous tablets, quick dissolving tablets, fast dissolving tablets etc., (Bi, Yonezawa and Sunada 1999) are those when put on tongue disintegrate instantaneously releasing the drug, which dissolve or disperses in the saliva (Ghosh, Ghosh and Prasad 2011). The advantage of mouth dissolving dosage forms are increasingly being recognized in both industry and academics (Hannan et al. 2016). Their growing importance was underlined recently when European pharmacopoeia adopted the term "orodispersible tablet" as a tablet that to be placed in the mouth, which get dispersed or disintegrate when gets in a contact with saliva with the release of active drug, where it disperses rapidly before swallowing. According to European pharmacopoeia, the ODT should disperse/disintegrate in less than three minutes (Fu Y et al. 2004).

MATERIALS AND EQUIPMENTS

Materials

Amlodipine (AMD) was gift sample from Aurobindo Pharmaceuticals, Hyderabad, India. Superdisintegrants such as sodium starch glycolate (SSG), cross carmalose sodium (CCS), cross povidone (CP) were from Amishi Drugs and Chemicals Ltd., Ahmedabad, India. Other superdisintegrants like ludiflash and isabgol from BASF Chemical Company, Germany and Indian Ayurverdic stores respectively. Taste masking agents like citric acid from Paragon Chemicals, India and menthol from Silverline Chemicals, Haryana, India. Aspartame from Nutra Sweet Ltd, India and orange from Bush Boake Allen Ltd, aerosil and magnesium stearate from Sd fine-Chem Limited, Mumbai, India.

Methods

Development of standard calibration curve

Amlodipine besylate (AMD) is a white crystalline powder. It is slightly soluble in water and sparingly soluble in ethanol. Stock solutions were prepared using ethanol and the final concentration (5, 10, 15, 20, 25, 30, 35, 40 µg/ml) were prepared from secondary stock solution. After thorough shaking for 10 minutes the volumetric flasks are set aside for 10 minutes. The absorbance of each sample was measured at 244nm against reagent blank (0.1N HCl) using UV visible spectrophotometer (Elico) (Indian Pharmacopoeia, 2007)

Preparation of amlodipine orodispersible tablets

Direct compression method

The drug and all other excipients were accurately weighed and sifted through #40 sieves and mixed thoroughly. The above blend was lubricated with aerosol and finally with magnesium state. The above lubricated blend was compressed using 6 mm standard flat-faced punch on a 16-station rotary tablet-punching machine (Cadmac).

Pre-evaluation studies

FTIR Studies:

The FT-IR spectrums of pure drug and with superdisintigrents were determined. A FT-IR (Bruker spectrometer) was used for the analysis in the frequency range between 4000 and 400 cm^{-1} resolution.

Differential scanning calorimetric study (DSC)

Thermal properties of pure drug and with superdisintigrents were evaluated by Differential scanning calorimetry (DSC) using a Diamond DSC (Mettler Star SW 8.10). The analysis was performed at a rate 5^0C min^{-1} from 50^0C to 200^0C temperature range under nitrogen flow of 25 ml min^{-1}.

Post-evaluation of tablets

All the formulated (F1 to F19) amlodipine orodispersible tablets were subjected to the following quality control tests (Lachman, Liberman and Kanig 1987; Banker 1987):

Weight variation (n=20)

Twenty tablets were selected at a random and then the average weight was determined. All the 20 tablets were weighed individually and compared with the average weight the tablets meet USP specifications if no more than 2 tablets are outside the percentage limit and if no tablet differs by more than 2 times the percentage limit.

Thickness of tablet (n=10)

Thickness is measured by using instrument called "Vernier calipers". Randomly ten tablets were taken and thickness was measured for each tablet by placing between two anvils and rotating sliding knob until the tablet was tightly fitted and the reading was noted on the scale.

Friability (n=20)

The friability test was performed for all the formulated amlodipine orodipersible tablets. Twenty tablets were taken and their weight was determined. Then they were placed in the Roche friabilator and allowed to make 100 revolutions. The tablets were then dedusted and reweighed. The percentage weight loss were calculated

% Friability was calculated as follows

$$\% \text{ Friability} = (W_1 - W_2) \times 100/W_1$$

Where, W1 = Initial weight of the 20 tablets. W_2 = Final weight of the 20 tablets after testing. Friability values below 1% are generally acceptable.

Hardness (n=6)

Monsanto hardness tester was used for measuring the hardness of the formulated orodipersible amlodipine tablets. From each batch six tablets were taken and subjected to test. The mean of the six tablets were calculated. The breaking strength (in kg) of each tablet was tested using a Stokes Monsanto hardness tester (DT Stokes, Bristol, PA). After the dial on the tester was set to zero, a tablet was placed between the two jaws. The breaking point was determined by gradually increasing the force on the tester. Breaking strength is the force applied (in kg) to break the tablet radially into two halves.

Assay (n=6)

Six tablets were taken, powdered well and a quantity of powder equivalent to 100 mg of amlodipine was accurately weighed and dissolved in 100 ml of 0.1N HCl and filtered. 10 ml of this solution was taken and diluted to 100 ml with 0.1N HCl. From this solution 1 ml was taken and diluted to 10 ml with 0.1N HCl. The absorbance of the solution was measured at 244 nm against blank (0.1N HCl). The concentration of the sample was calculated using standard graph.

***In vitro* disintegration time (n=3)**

In vitro disintegration time (DT) for amlodipine ODTs (n=3) were determining using USP disintegration apparatus with 0.1N HCl as disintegrating medium.

Wetting Time (n=3)

The wetting time of the tablets (n=3) was measured using a simple procedure. Five circular tissue papers of 10 cm diameter were placed in a Petri dish containing 10.0 ml of water containing eosin blue. A tablet was carefully placed on the surface of tissue paper. The time required for develop blue colour on the upper surface of the tablet was noted as the wetting time.

***In vitro* drug release studies (n=6)**

In vitro dissolution studies for all the formulated orodispersible tablets was carried out using USP Type-II method at 75 rpm in 500ml of 0.1N HCl as dissolution medium, maintained at 37±0.5 ^{0}C. 5 ml aliquot was withdrawn at the specified time intervals, filtered through whatmann filter paper and assayed spectorphotometrically at 244 nm (Indian Pharmacopoeia 2007). An equal volume of fresh medium, which was pre warmed at 37 ^{0}C, was replaced into the dissolution media after each sampling to maintain the constant volume throughout the test.

***In vivo* disintegration time (n=3)**

The *in vivo* disintegration time was taken on the 3 healthy human volunteers, the tablet kept in the mouth after rinsing and the time required for complete disintegration of the tablet was recorded.

***In vivo* taste and flavor evaluation (n=3)**

Mouth feel is critical, depends upon taste, flavors were used. The formulated amlodipine ODT can administer as 'Direct tablet' the tablet is placed on the tongue, the tablet disintegration and mouth feel was recorded. *In vivo* taste and flavor evaluation were conducted on three selected age group of the people having 30-35 years male volunteers. For taste evaluation the tablets prepared with sweetening agent such as aspartame was given individually for the different subjects and for flavor evaluation the tablets prepared with orange flavor given individually to different subjects.

RESULTS AND DISCUSSION

Results

UV spectrophotometric method was developed for the amlodipine (AMD). The method obeyed Beer's law in the concentration of 5-40 µg/ml with regression coefficient of 0.9941. Thus the said method was found to be suitable for the estimation of amlodipine *in vitro* dissolution studies.

Fourier transforms infrared spectroscopy (FT-IR)

Infrared spectroscopy is one of most powerful analytical technique when it comes to the determination of presence of various functional groups involved in making up the molecule. It provides very well account table spectral data regarding any change in the functional group characteristics of a drug molecule occurring while in the processing of formulation. IR spectra of amlodipine and its formulations were obtained by KBr pellet method using Bruker spectrophotometer in order to rule out drug carrier interaction occurring during the formulation process and results were shown in Fig.1.

Differential scanning calorimetric study

The drug excipients compatibility study was carried out by using DSC. The thermal properties of the drug and the mixture of drug and excipients are of important interest since this can help to assess the interaction among different components of the formulations. The DSC thermograms (Fig. 2) of pure drug (amlodipine) (A), with CP (B), with CCS (C), with ludiflash (D) and with isobgul (E) showed sharp endothermic peaks at 209.98 ^{0}C, 206.12 ^{0}C, 208.19 ^{0}C, 206.11 ^{0}C and 204.52 ^{0}C respectively.

Formulation of amlodipine orodispersible tablets

Initially amlodipine ODT (Table 1) were developed with different superdisintegrants, SSG (F1), CCS (F2), CP (F3), ludiflash (F4) and isobgul (F5) containing 5% concentration in each formulation. Physical characters and *in vitro* dissolution data of amlodipine ODT (F1-F4) was shown in Table 2. Even though tablets releasing 90-100% drug in 15min. the disintegration time is more. As per USFDA guidelines ODT tablets, the tablets should disintegrate in less than 30 seconds, it should directly reflect on the mouth disintegration. The drug release profiles were shown in Fig.3. Based on these considerations it was decided to increase the concentration of superdisintegrants in the further study.

The amlodipine ODT (Table 3) were developed with increased concentration of superdisintegrants (up to 7.5%), SSG (F6), CCS (F7), CP (F8), ludiflash (F9) and isobgul (F10) containing 7.5% concentration in each formulation to improve the disintegration time. Physical characters and *in vitro* dissolution data of amlodipine ODT (F6-F9) was shown in Table 4. The drug release profiles were shown in Fig.4. The amlodipine ODT (Table 5) were developed with increased concentrations of superdisintegrants, SSG (F11), CCS (F12), CP (F13), ludiflash (F14) and isobgul (F15) containing 10% concentration in each formulation to improve the disintegration time. Physical characters and in vitro dissolution data of amlodipine ODT (F11-F15) were shown in Table 6. The drug release profiles were shown in Fig.5.

Based on the above results it was clearly observed that the above formulations improved the disintegration time with increased concentration of superdisintegrants. The above tablets were tested for *in vivo* disintegration time in mouth. During mouth disintegration the tablets prepared with SSG, CP gives smooth mass and disintegrates in 9.3±1.6 and 9.26±1.42 seconds respectively. The tablets prepared with ludiflash disintegrate in 23.83±1.29 seconds and gives smooth, foamy like feeling in the mouth. So, it was decided to incorporate the ludiflash along with other superdisintegrants for further study. Based on the *in vitro* disintegration time from the previous study (F1-F15), amlodipide ODT were developed by using combination of superdisintegrats F16-F17 by using SSG (5%), CP (5%) with combination of ludiflash (5%) for improve disintegration time and the formulae was shown in Table 7. Physical characters and in vitro dissolution data of amlodipine ODT's (F16-F17) were show in Table 8. The drug release profiles were shown in Fig.6.

Sweetener, flavour was added to the formulation to mask the bitter taste and to enhance mouth feel of amlodipine respectively. Sweeteners such as aspartame, flavour such as orange flavour was incorporated in the formulation (F18-F19). Along with sweetener, flavour, citric acid and menthol also incorporated for improved taste and mouth feel. Sweeteners such as aspartame, flavor such as orange flavour were incorporated to the above formulations (F16-F17) and developed F18-F19 and the formulae shown in Table 9. Physical characteristics, *in vitro* dissolution data and including mouth feel of amlodipine ODT (F18-F19) were shown in Table 10. The drug release profiles were shown in Fig.7.

Discussion

Amlodipine orodispersible tablets were developed with an aim to improve the patient compliance and to improve bioavailability. The formulations (F1-F19) were developed with an objective to use by the paediatric, geriatric, bedridden and psychotic patients. DSC and FTIR studies showed no drug excipient interaction. The development was initiated with standard calibration curve using UV spectrophotometric methods as it is required to routine analysis of the drug. The UV spectrophotometric method was developed in 0.01N HCl at 244 nm.

The method shows linearity in the range of 5-40 µg/ml with a correlation coefficient (R^2) of 0.994. Initially formulation developed with different superdisintegrants such as SSG, CCS, CP, ludiflash and isabgol. 5% of the superdisintegrants were used in each formulation. The formulations (F1-F5) yields rapid disintegration and dissolutions. However disintegration time (DT) was a little more in the above formulations. For improvement of disintegration time, the formulations were prepared with increased concentration form 5% to 7.5% (F6-F10) and 7.5% to 10% (F11-F15) of superdintegrants for improved the disintegration time. The formulations prepared with Ludiflash also prove less disintegration time. The tablets were compressed using 6 mm round punch with 100 mg of tablet weight of 100mg. The prepared tablets were evaluated for different physical properties like weight variation, thickness, friability and disintegration time, hardness, wetting time, assay and *in vitro* dissolution studies. The weight variation of all the formulations was within the range. The drug content of amlodipine from all the formulations was found in the range of 98% to 99%. The hardness was found between 3.5 to 4.0 kg/cm^2 (F1-F19) and friability for all the formulation shown less than 0.90% which is in the acceptable limits which indicates formulations have good mechanical strength. Thickness of the tablets found to be 2.64 ± 0.06 mm (F16) to 2.94 ± 092 mm (F19).

Disintegration time of formulations (F1-F5) containing with 5% in each formulation SSG (F1), CCS (F2), CP (F3), ludiflash (F4) and isobgul (F5) were found between 36.04 ± 1.4 (F2) to 45.58 ± 1.5 (F4) seconds. Disintegration time of formulations (F6-F10) containing with 7.5% in each formulation SSG (F6), CCS (F7), CP (F8), ludiflash (F9) and isabgol (F10) were found between 18.81±0.98 (F8) to 39.14 ± 1.6 (F9) seconds. And disintegration time of formulations (F11-F15) containing with 10% in each formulation SSG (F11), CCS (F12), CP (F13), ludiflash (F14) and isabgol (F15) found to be 9.3 ± 1.6 (F11) to 23.83 ± 1.29 (F14) seconds. Wetting time in above formulations found to be between 41 ± 2.8 (F6) to 49 ± 3.2 (F9) seconds. The results were summarized in Table 2, 4, 6, 8 and 10. Based on physical properties like weight variation, thickness, hardness, friability, disintegration time, wetting time, assay and *in vitro* dissolution studies. The drug release profiles were shown in Fig. 3, 4, 5, 6 and 7. Based on physical properties and *in vitro* drug release profiles (F16-F17) formulations were prepared with SSG, CP resulted smooth and fine particles, where as the formulations prepared with in combination with ludiflash yields creamy, foam like mass. From the above results F16 and F17 formulations were selected as best formulations.

Table 1: Formulation data for amlodipine ODT with different superdisintegrants containing 5% concentration in each formulation

Ingredients	F1	F2	F3	F4	F5
	mg/tablet				
AMD	10	10	10	10	10
SSG	5		-	-	-
CCS	-	5	-	-	-
CP	-	-	5	-	-
Ludiflash	-	-	-	5	-
Isabgol	-	-	-	-	5
MCC-PH 200	75	75	75	75	75
Aerosil	6	6	6	6	6
Talc	3	3	3	3	3
Mg. Stearate	1	1	1	1	1
Tablet weight	100	100	100	100	100

Table 2 Physical characters and *in vitro* dissolution data of amlodipine ODT with different superdisintegrants containing 5% concentration in each formulation

Parameter	F1	F2	F3	F4	F5
Weight Variation [a]	100.1±1.2	101±1.5	102±1.7	101±1.5	101±1.7
Thickness [b]	2.78±0.02	2.84±0.03	2.81±0.03	2.86±0.04	2.79±0.02
Friability [a]	0.47	0.58	0.78	0.43	0.59
Hardness [c]	5±0.5	5±0.5	5±0.5	5±0.5	5±0.5
Disintegration time [d] (sec.)	39.49±1.1	36.04±1.4	38.6±1.2	45.58±1.5	40.9±1.3
Wetting time [d] (sec.)	52±2.8	56±1.8	50±2.5	58±1.5	57±1.1
Assay [c] (%)	99±1.3	98±1.23	99±1.5	98±0.9	98±1.34

[a] Each value represents mean ± S.D (n=20); [b] Each value represents mean ± S.D (n=10); [c] each value represents mean ± S.D (n=6); [d] each value represents mean ± S.D (n=3).

Table 3: Formulation data for amlodipine ODT with different superdisintegrants containing 7.5% concentration in each formulation

Ingredients	F6	F7	F8	F9	F10
	mg/tablet				
AMD	10	10	10	10	10
SSG	7.5		-	-	-
CCS	-	7.5	-	-	-
CP	-	-	7.5	-	-
Ludiflash	-	-	-	7.5	-
Isabgol	-	-	-	-	7.5
MCC-PH 200	72.5	72.5	72.5	72.5	72.5
Aerosil	6	6	6	6	6
Talc	3	3	3	3	3
Mg. Stearate	1	1	1	1	1
Tablet weight	100	100	100	100	100

Table 4: Physical characters and *in vitro* dissolution data of amlodipine ODT with different superdisintegrants containing 7.5% concentration in each formulation

Parameter	F6	F7	F8	F9	F10
Weight Variation [a]	100.3±1.8	102±1.67	102±1.9	101.5±1.7	100.54±1.68
Thickness [b]	2.78±0.02	2.81±0.03	2.92±0.02	2.87±0.06	2.84±0.04
Friability [a]	0.56	0.64	0.87	0.51	0.64
Hardness [c]	3.5±0.5	4.0±0.5	3.5±0.5	4±0.5	4±0.5
Disintegration time [d] (sec.)	25.9±1.2	28.5±1.56	18.81±0.98	39.14±1.6	23.09±1.48
Wetting time [d] (sec.)	41±2.8	46±1.7	43±3.2	49±3.2	47±1.8
Assay [c] (%)	99±0.56	98±0.42	99±0.59	98±1.23	98±1.52

[a] Each value represents mean ± S.D (n=20); [b] Each value represents mean ± S.D (n=10); [c] each value represents mean ± S.D (n=6); [d] each value represents mean ± S.D (n=3).

Table 5: Formulation data for amlodipine ODT with different superdisintegrants containing 10% concentration in each formulation

Ingredients	F11	F12	F13	F14	F15
	mg/tablet				
AMD	10	10	10	10	10
SSG	10		-	-	-
CCS	-	10	-	-	-
CP	-	-	10	-	-
Ludiflash	-	-	-	10	-
Isabgol	-	-	-	-	10
MCC-PH 200	70	70	70	70	70
Aerosil	6	6	6	6	6
Talc	3	3	3	3	3
Mg. Stearate	1	1	1	1	1
Tablet weight	100	100	100	100	100

Table 6: Physical characters and *in vitro* dissolution data of amlodipine ODT with different superdisintegrants containing 10% concentration in each formulation

Parameter	F11	F12	F13	F14	F15
Weight Variation [a]	100.2±1.8	100±1.8	101±1.6	102±1.4	102±1.5
Thickness [b]	2.8±0.09	2.8±0.08	2.7±0.09	2.9±0.07	2.8±0.065
Friability [a]	0.68	0.72	0.92	0.65	0.73
Hardness [c]	3.5±0.5	4±0.5	3.5±0.5	4±0.5	3.5±0.5
Disintegration time [d] (sec.)	9.3±1.6	12.57±1.32	9.26±1.42	23.83±1.29	15.6±1.47
Wetting time [d] (sec.)	42±1.9	45±2.1	42±1.6	45±3.2	48±1.85
Assay [c] (%)	99±1.2	99±0.98	99±0.65	99±1.52	99±1.54

[a] Each value represents mean ± S.D (n=20); [b] Each value represents mean ± S.D (n=10); [c] each value represents mean ± S.D (n=6); [d] each value represents mean ± S.D (n=3).

Table 7: Formulation data for amlodipine ODT with 5% SSG, 5% CP in combination with 5% ludiflash

Ingredients	F16	F17
	mg/tablet	
AMD	10	10
SSG	5	-
CP	-	5
Ludiflash	5	5
MCC-PH 200	70	70
Aerosil	6	6
Talc	3	3
Mg. Stearate	1	1
Tablet weight	100	100

Table 8: Physical characters and *in vitro* dissolution studies of amlodipine ODT with 5% SSG, 5% CP in combination with 5% ludiflash

Parameter	F16	F17
Weight Variation [a]	101.3±1.2	100.8±1.67
Friability [a]	0.82	0.89
Hardness [c]	3±0.5	3.5±0.5
Thickness [b]	2.64±0.06	2.71±0.06
Disintegration time [d] (sec.)	13.21±1.2	12.89±1.6
Wetting time [d] (sec.)	46±2.8	42±1.78
Assay [c] (%)	99±1.08	99±1.02

[a] Each value represents mean ± S.D (n=20); [b] Each value represents mean ± S.D (n=10); [c] each value represents mean ± S.D (n=6); [d] each value represents mean ± S.D (n=3).

Table 9: Formulation data for amlodipine ODT with 5% SSG, 5% CP in combination with 5% ludiflash along with aspartame sweetener and orange flavour

Ingredients	F18	F19
	mg/tablet	
AMD	10	10
SSG	5	-
CP	-	5
Ludiflash	5	5
Citric acid	2	2
Menthol	1	1
Aspartame	2	2
Orange	1	1
MCC-PH 200	64	64
Aerosil	6	6
Talc	3	3
Mg. Stearate	1	1
Tablet weight	100	100

Table 10: Physical characters and *in vitro* dissolution data of amlodipine with 5% SSG, 5% CP in combination with 5% ludiflash along with aspartame sweetener and orange flavour

Parameter	F18	F19
Weight Variation [a]	100.6±1.23	100.1±1.62
Thickness [b]	2.89±0.58	2.94±0.92
Friability [a]	0.84	0.88
Hardness [c]	3.5±0.5	3.5±0.5
Disintegration time [d] (sec.)	13.81±1.2	13.08±1.6
Wetting time [d] (sec.)	47±1.6	45±1.8
Assay [c] (%)	99.56±0.32	99.53±0.82
Taste/Mouth feel [d]	Excellent	Excellent

[a] Each value represents mean ± S.D (n=20); [b] Each value represents mean ± S.D (n=10); [c] each value represents mean ± S.D (n=6); [d] each value represents mean ± S.D (n=3).

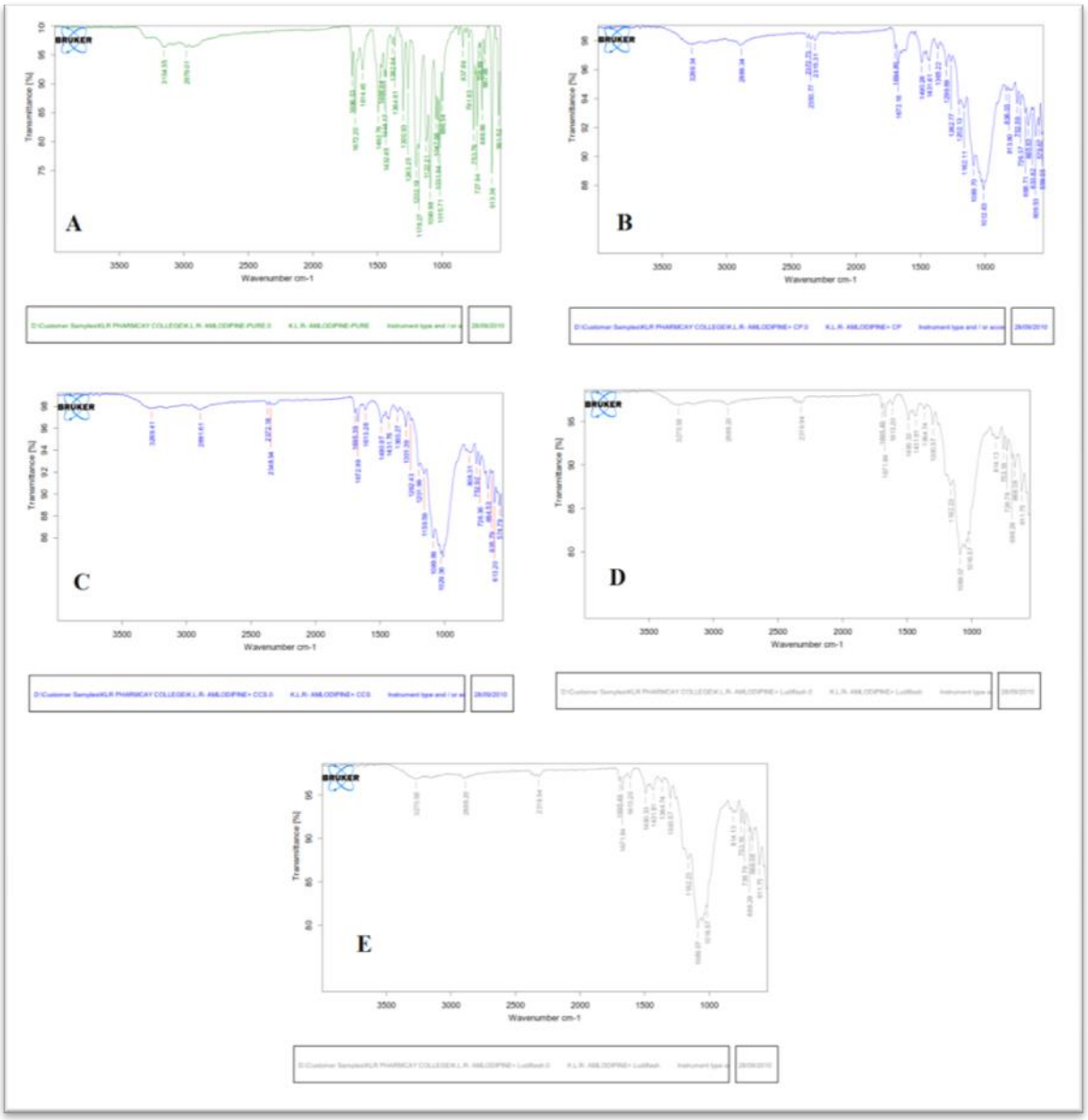

Fig.1: FT-IR studies of pure drug and with different superdisintigrents: A) Pure drug (AMD); B) mixture of amlodipine and CP; C) mixture of amlodipine and CCS; D) mixture of amlodipine and ludiflash; E) mixture of amlodipine and isobgul

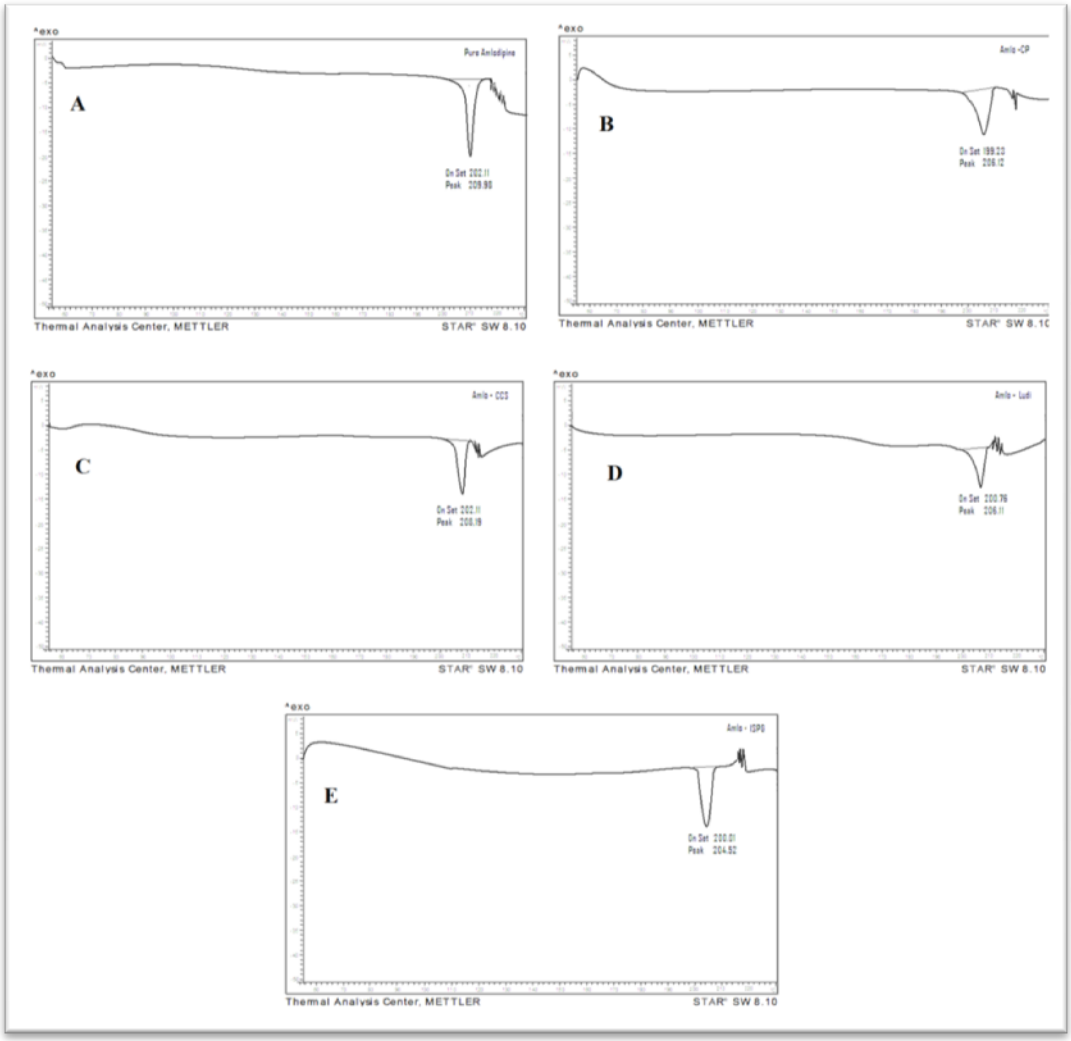

Fig. 2: DSC thermograms of pure drug and with different superdisintigrents: A) Pure drug (AMD); B) mixture of amlodipine and CP; C) mixture of amlodipine and CCS; D) mixture of amlodipine and ludiflash; E) mixture of amlodipine and isobgul

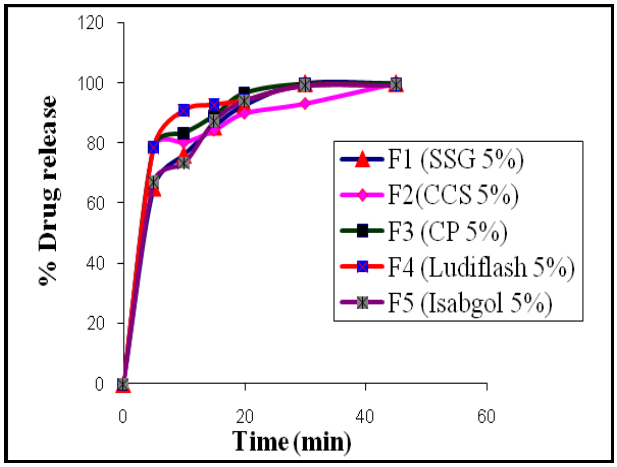

Fig. 3: Cumulative % drug release profiles of amlodipine ODT prepared with different superdisintegrants containing 5% concentration in each formulation

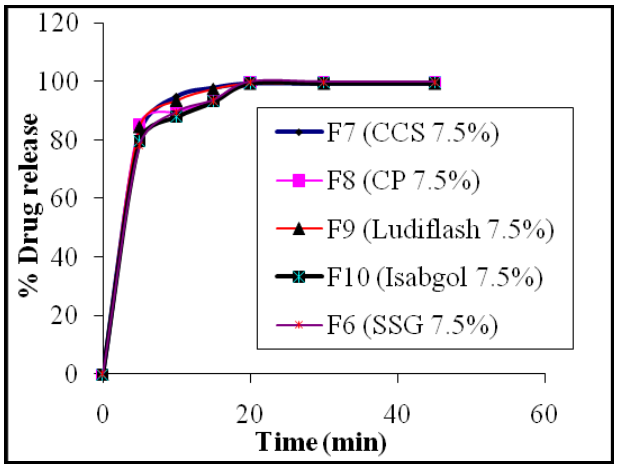

Fig. 4: Cumulative % drug release profiles of amlodipine ODT prepared with different superdisintegrants containing 7. 5% concentration in each formulation

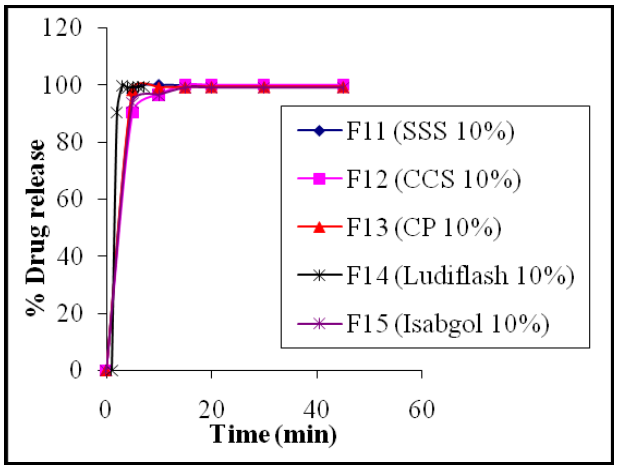

Fig. 5: Cumulative % drug release profiles of amlodipine ODT prepared with different superdisintegrants containing 10% concentration in each formulation

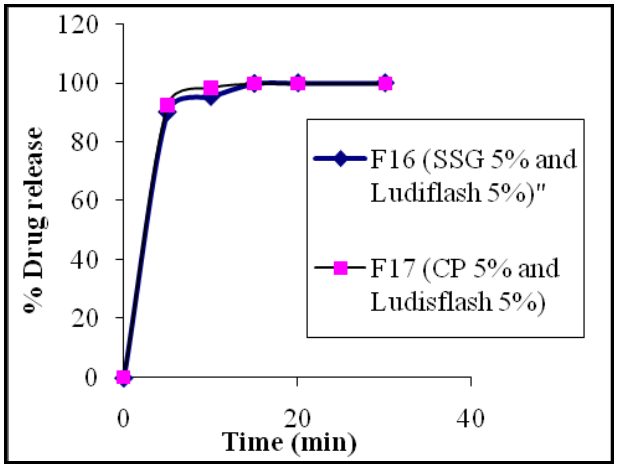

Fig. 6: Cumulative % drug release profiles of amlodipine ODT prepared with 5% SSG, 5% CP in combination with 5% ludiflash

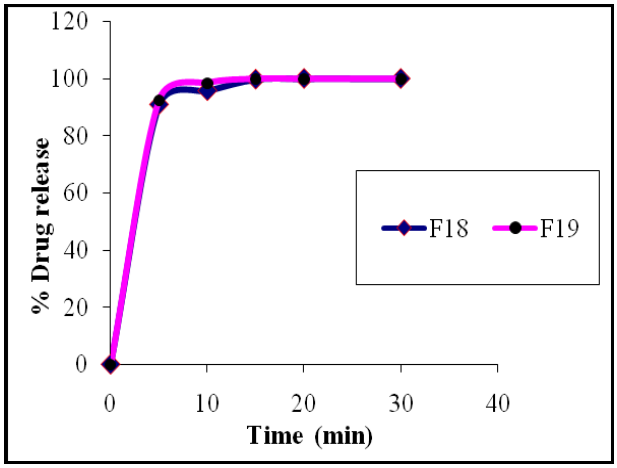

Fig. 7: Cumulative % drug release profiles of amlodipine ODT prepared with 5% SSG, 5% CP in combination with 5% ludiflash along with aspartame sweetener and orange flavour

For improvement of taste and mouth feel add orange flavour and aspartame sweetener along with citric acid and menthol were added to above formulations (F16 and F17) and developed F18 and F19. There are no changes in physical properties observed for the formulations prepared with SSG, CP in combination with ludiflash, aspartame and orange flavour. The formulations (F18-F19) score excellent during *in vitro* and *in vivo* evaluation. So, F18 and F19 formulations were selected as optimized formulations.

CONCLUSION

Orodispersible tablets of amlodipine were successfully developed using direct compression method by incorporating different superdisintegrants in different concentrations. From the results F16 and F17 formulations containing SSG (5%), CP (5%) and ludinflash (5%) should fast dissolution in contrast to other formulations. Based on better mouth feel and patient compliance F18-F19 formulations were optimized. Hence it can be concluded that using a combination of superdiintegrants viz., SSG, CP and ludiflash in the ratio of 1:1:1 in the formulation of orally disintegrating tablets of Amlodinpine would be quite effective in providing fast onset of action without the need of water for swallowing.

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