**RESEARCH ARTICLE**

# Development of Floating Tablet of Amlodipine Besylate for Bioavailability Improvement in Animal Model

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## ABSTRACT

**Objective:** Floating drug delivery system is developed for Amlodipine Besylate to improve bioavailability in animal models using different combinations of polymer and excipients.

**Significance:** Increased blood plasma concentration of the drug compared to existing marketed tablets of the drug improves efficacy.

**Methods:** Floating tablet formulations of the drug were prepared using combinations of polymer and excipients. Average weight, thickness, disintegration, dissolution, and Assay of formulations containing different composition were carried out. The stable, evaluated optimized formulations were subjected to in vivo drug bioavailability in a rat model.

**Results:** Based on the post-compression parameter, buoyancy lag time, total floating time and cumulative %drug release, the optimized formulations were selected. An optimized formulation containing combination of excipients showed good stability and comparative more plasma concentration of the drug in animal model.

**Conclusions:** Floating tablets of Amlodipine besylate were developed to get optimum tablet properties and drug content. The absorption of amlodipine from formulation resulted in multi fold increase in bioavailability as compared to marketed tablets.

**Keywords:** Amlodipine Besylate, Bioavailability, Eudragit, Floating drug delivery, HPMC.

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## INTRODUCTION

The challenge to develop efficient gastro-retentive dosage forms began about twenty years ago. The gastroretentive systems can be of different types such as high-density systems, low density systems, gas generating systems, floating drug delivery systems or hydrodynamically balanced systems, raft forming systems, expandable systems, super-porous hydrogels, mucoadhesive systems and magnetic systems.[1] Floating drug delivery system was first described by Davis in 1968. [2,3] The floating drug delivery system can stay in the stomach for a long time, and other content will not affect gastric emptying rate.[4] The floating dosage form is very useful for drugs that act locally in the proximal gastrointestinal tract (GIT),[5] and is unstable in the lower parts of GIT,[6] or has maximum absorption in the upper part of GIT.[7] When designing such systems an important consideration is to ensure that they remain in the upper gastrointestinal tract until all drugs are released within the desired period.[8]

In recent years, especially in the past two decades, many technologies and scientific research have been devoted to the development of rate controlled oral drug delivery system to overcome physiological problems, such as short gastric residence times (GRT) and unpredictable gastric emptying times (GET), in order to be able to formulate gastroretentive dosage forms, which will allow the delivery of drug with a limited 'absorption window' can be absorbed in a specific part of gastrointestinal tract. Various approaches are currently being used to prolong the GRT, includes floating drug delivery system (FDDS), also known as hydrodynamically balanced system (HBS), swelling and expanding systems,

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high-density systems, and other delayed gastric emptying devices.[9]

Hypertension is the main cause of high blood pressure in the elderly. The incidence rate increases with age. Long-acting dihydropyridines such as amlodipine are very effective antihypertensive drugs for the treatment of ISH in the elderly due to their vasodilation and negative ionotropic effect.[10]

Amlodipine is a long-acting calcium channel blocker used to treat hypertension and chronic stable angina pectoris. For hypertension or angina pectoris, 5 mg is initially prescribed, amlodipine is taken orally every day (maximum dose is 10 mg). Amlodipine has maximum solubility in acidic pH. Amlodipine has some side effects, such as nausea and abdominal pain. Amlodipine besylate effervescent floating tablet retains in the stomach can improve solubility and bioavailability, reduces drug waste, and reduce side effects, such as gastric irritation and nausea.[12] It is well absorbed after oral administration and has a bioavailability of around 60–65%.[13]

In the present work, amlodipine besylate effervescent floating tablets were developed with the objective of achieving maximum floating, bioavailability, and drug release time. It is also indicated in the treatment of vasospastic angina pectoris and chronic stable angina pectoris. Amlodipine Besylate floating tablets 10mg is formulated as a tablet for oral administration. It is a white, circular tablet that contains Amlodipine Besylate USP equivalent to Amlodipine10mg with commonly used excipients.

This report contains information and data on development studies conducted to establish the dosage form, physicochemical and biological properties, and compatibilities of the tablets.

## MATERIALS AND METHODS

### Procurement of Material

Amlodipine Besylate requested from Kopran Limited as drug sample. Marketed 'AMLOSAFE' tablet (Amlodipine Besylate Tablets equivalent to 10 mg amlodipine) procure from Aristo Pharmaceuticals Pvt Ltd. Excipients used in the formulations are Eudragit-L-100 (Loba chemicals), HPMC K100M (Loba chemicals), Carbapol 934P (Himedia), Microcrystalline Cellulose (PH 102) (Loba chemicals), Sodium Bicarbonate (Loba chemicals), Citric Acid (Loba chemicals), Povidone K30 (Loba chemicals), Magnesium Stearate (Rajesh Chemicals), Purified Talc (Loba Chemicals), Aerosil (Himedia). De-ionized water prepared from Millipore was used.

### Method

*Selection of Excipient*

Excipients listed in Table 1 are selected according to their function as per literature. Criteria for the selection of excipients are prior knowledge and variability concerning the physicochemical and functional properties of all excipients used in formulation design and Excipient compatibility study.

### Compatibility Study of the Active substance (Drug) with Excipients

Compatibility study of active ingredient was carried out with the commonly used excipients under stressed conditions of 60ºC for 6 hours and 80°C for 30 minutes.[14-16] This aided in ruling out apparently incompatible excipients. A binary mixture of the drug and the excipients were prepared in 1:1 ratio. Results of the compatibility study of the drug with excipients used in the formulation of the drug product are given in Table 2.

### Development of Formulation Composition

The development of the qualitative and quantitative composition of the formulation was carried out and compared with the marketed 'Amlosafe' table. Extensive development and process qualification studies were carried out to evaluate the significance of changing process parameters on the quality and performance of the formulation. Developmental studies were initiated by taking into account the basic requirements of tablet compression (Dry mixing Method). The following procedure was adopted to prepare different formulations containing 13.87 mg of Amlodipine Besylate BP equivalent to 10 mg of amlodipine. All the materials mentioned were sifted through specified sieves (Sifting).[17] All the ingredients in the dry mix thoroughly in a planetary mixer for 15 minutes (Dry Mixing). The dried mix was mixed with the Magnesium Stearate BP and purified Talc BP thoroughly and uniformly and mix for 5 min. (Lubrication). Then lubricated blend was compressed into tablets as per specified tools and punches (Compression).

**Table 1:** Selection of Excipients Based on their Function in Formulation

| *Sr.* | *Name of the excipients* | *Literature reference* | *Functions* |
|---|---|---|---|
| 1. | Eudragit-L-100 | United States Pharmacopoeia | Anionic copolymer |
| 2. | HPMC K100M | British Pharmacopoeia & Handbook of Pharmaceutical Excipients 6th edition | Polymer |
| 3. | Carbopol 934P | British Pharmacopoeia & Handbook of Pharmaceutical Excipients 6th edition | Disintegrant |
| 4 | Microcrystalline Cellulose (PH 102) | British Pharmacopoeia & Handbook of Pharmaceutical Excipients 6th edition | Diluent |
| 5 | Sodium Bicarbonate | British Pharmacopoeia & Handbook of Pharmaceutical Excipients 6th edition | Gas forming agent |
| 6 | Citric Acid | British Pharmacopoeia & Handbook of Pharmaceutical Excipients 6th edition | Effervescent agent |
| 7 | Povidone K30 | British Pharmacopoeia & Handbook of Pharmaceutical Excipients 6th edition | Binder |
| 8 | Magnesium Stearate | British Pharmacopoeia & Handbook of Pharmaceutical Excipients 6th edition | Lubricant |
| 9 | Purified Talc | British Pharmacopoeia & Handbook of Pharmaceutical excipients 6th edition | Lubricant |
| 10 | Aerosil | Evonik Industries | Glidant |

**Table 2:** Compatibility of Amlodipine Besylate with excipients

| | | *Appearance* | *Observations* | |
|---|---|---|---|---|
| *Sr. No.* | *Amlodipine Besylate USP + Excipients* | *Initial (Color)* | *60°C for 6 hours* | *80°C for 30 min* |
| 1 | Eudragit-L-100 | White powder | White powder | white powder |
| 2 | HPMC K100M | White fluffy powder | No change | No change |
| 3 | Carbapol 934P | White powder | No change | No change |
| 4 | Microcrystalline Cellulose (PH 102) | White lump mass | No change | No change |
| 5 | Sodium Bicarbonate | White powder | No change | No change |
| 6 | Citric Acid | White fluffy powder | No change | No change |
| 7 | Povidone K30 | White powder | No change | No change |
| 8 | Magnesium Stearate | White powder | No change | No change |
| 9 | Purified Talc | White fluffy powder | No change | No change |
| 10 | Aerosil | White lump mass | No change | No change |

**Evaluation of Formulation**

Evaluation of different formulations and marketed tablets was carried out according to methods described[18] with slight modifications for different evaluation parameters, including physical evaluation, content uniformity, dissolution study, and release kinetics.

**Profile of Marketed 'Amlosafe' Tablet**

Amlosafe tablet of Aristo Pharmaceuticals Pvt Ltd. was studied to get a standard profile of the tablet. Average weight, thickness, disintegration, dissolution and Assay were carried out.

**Evaluation of formulations**

Average weight, thickness, disintegration, dissolution and Assay of formulations containing different compositions were carried out.

**Stability Study**

Stability study of trial IX (Formulation F9) for long term (30°C/65%RH) and accelerated (40°C/75%RH) was carried outpost 3 and 6 months of the formulation.[19]

***In vivo* Bioavailability Study of Amlodipine in the Formulation**

Male Wistar rats of either sex weighing round 220-250 gm obtained from Animal house facility, Serum Institute of India Pvt. Ltd, Pune were used for study. An institutional animal ethics committee approved the experimental protocol for this study (IAEC; Ref. No. 448/01/c/CPCSEA/PRCOP/2014-15/17) according to CPCSEA guidelines. Animal were housed in cages of slandered dimensions with sawdust (dust-free corncob) bedding. The animals were housed in controlled environmental conditions in which recycled, filtered air was changed approximately 20 times per hour. Standard pelleted rodent chow feed was given ad libitum except during the experimental fasting period. Drinking water was available ad libitum in polycarbonate feeder bottles with stainless steel nipple.

The animals were maintained under the standard environmental conditions and were fed with a standard diet and water *ad libitum*. The animal's were fasted for 18 hours before the experiment but allowed free access to water.[20] Animals (n = 6) were divided into two groups. Group I received amlodipine at a dose of 1mg/kg body weight in water. Group II were given the innovator drug. Blood samples were taken at time interval followed by centrifuged immediately at 1600g. Plasma was stored at -20°C until analysis. The analysis was performed using gradient high-performance liquid chromatographic system. The data obtained from HPLC was treated to get AUC.

**Statistical Analysis**

Values are expressed as means ± SD (Standard deviation). Statistical analysis was performed by on way ANOVA followed by Dunnett's test using graph pad instant software version 3.0 to find the differences between the groups. $P < 0.05$ was considered as statistically significant.

## RESULTS

**Selection of the Excipient**

Excipients, including polymers and additives as given in table 1 were selected for their proper use in formulations.

**Compatibility Study of the Active Substance (Drug) with Excipients**

In the compatibility study of the drug with excipients, no any physical changes were observed when exposed to 60°C for 6 hours and 80°C for 30 minutes. The ingredients do not show any incompatibility with the drug and hence used for further study as shown in Table 2. Spectral data of all excipients, physical mixture and drugs alone were carried out as shown in Figures 1 to 6.

**Development of Formulation Composition**

The development of amlodipine besylate floating tablets comprised knowledge on the variability with respect to physicochemical and functional properties in all excipients used in the formulation design. Different trial formulations are described in Table 3 to prepare different formulations containing 0 mg of amlodipine. In the development of floating tablets, citric acid and sodium bicarbonate are functioning ingredients for the release of drugs in acidic gastric medium. Compositions of these ingredients were chosen according to the literature. Key changes in formulation excipients we have

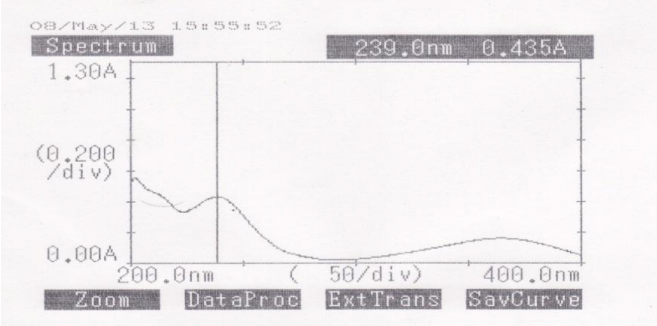


**Figure 1:** Absorption maximum (λmax) was found to be 239 nm.

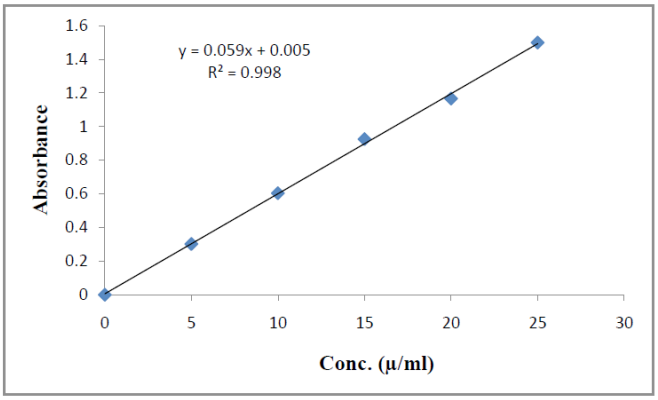


**Figure 2:** Calibration curve for amlodipine in 0.1N HCl.

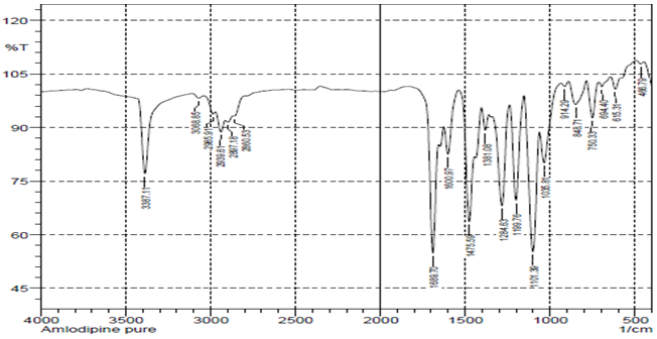


**Figure 3:** FTIR spectra of pure amlodipine.

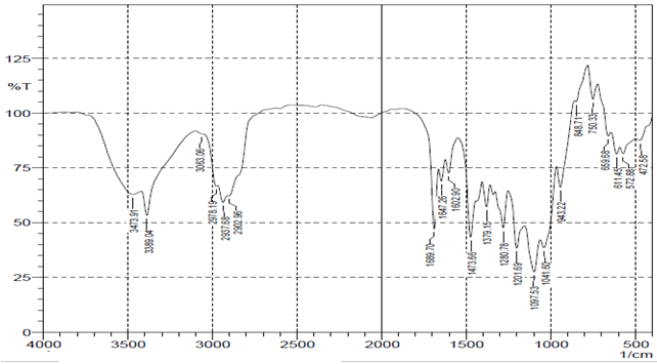


**Figure 4:** FTIR spectra of Amlodipine and HPMC K 100 M + Eudragit L 100.

made were eudragit, HMPC, carbopol, and MCC composition. Various combinations of these ingredients with 15, 30 and 45 mg were taken and studied effect of these polymers on an effective formulation.

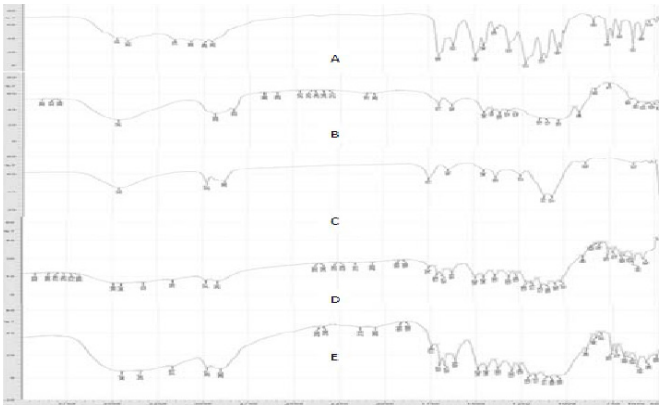


**Figure 5:** The FT-IR spectra for (A) pure amlodipine; (B) HPMC K 100 M; (C) Eudragit L 100; (D) Physical mixture; (E) Amlodipine Besylate floating freeze tablet

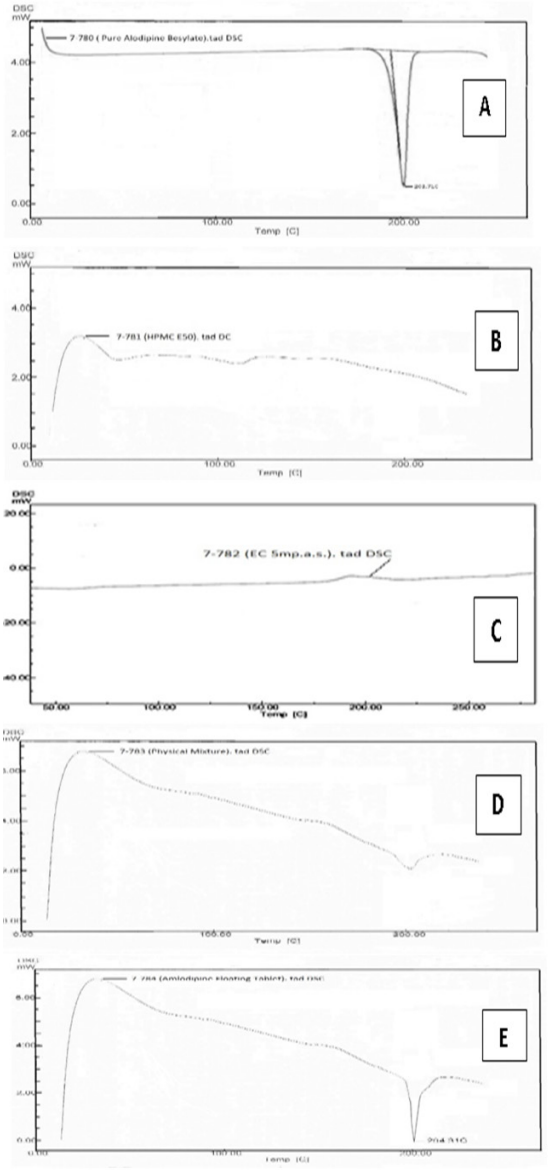


**Figure 6:** Differential Scanning Calorimetry thermograms of (A) Pure Amlodipine, (B) HPMC K 100, (C) Eudragit L 100, Physical mixture (D) and amlodipine floating freeze tablet (E)

**Table 3:** Composition of trial formulation

| *Ingrdient* | *F1 (mg)* | *F2 (mg)* | *F3 (mg)* | *F4 (mg)* | *F5 (mg)* | *F6 (mg)* | *F7 (mg)* | *F8 (mg)* | *F9 (mg)* |
|---|---|---|---|---|---|---|---|---|---|
| Amlodipine besylate USP | 13.87 | 13.87 | 13.87 | 13.87 | 13.87 | 13.87 | 13.87 | 13.87 | 13.87 |
| Eudragit-L-100 USP | 15 | 15 | 15 | 30 | 30 | 30 | 45 | 45 | 45 |
| HPMC K100M BP | 15.13 | 30.13 | 45.13 | 15.13 | 30.13 | 45.13 | 15.13 | 30.13 | 45.13 |
| Carbapol 934P BP | 45 | 45 | 45 | 30 | 30 | 30 | 15 | 15 | 15 |
| MCC (Ph 102) BP | 45 | 30 | 15 | 45 | 30 | 15 | 45 | 30 | 15 |
| Sodium bicarbonate BP | 30 | 30 | 30 | 30 | 30 | 30 | 30 | 30 | 30 |
| Citric acid BP | 25 | 25 | 25 | 25 | 25 | 25 | 25 | 25 | 25 |
| Povidone K30 BP | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |
| Magnesium stearate BP | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |
| Purified talc BP | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 |
| Aerosil | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| Total weight | 205 | 205 | 205 | 205 | 205 | 205 | 205 | 205 | 205 |

**Table 4:** Profile of Marketed 'Amlosafe' Tablet

| *Parameters* | *Description* |
|---|---|
| Composition<br>(Each Uncoated tablet contains) | Amlodipine Besylate USP equivalent to Amlodipine 10.0 mg ($C_{20}H_{25}N_2O_5Cl$)<br>Batch No. - A01838 (10 tablets in Blister pack) |
| Description | Off white-colored circular, flat, beveled edged tablet with break line on one side and "A P" printed on the other side. |
| Average Weight/tablet | 232.0 mg |
| Thickness | 4.0 mm |
| Disintegration Time | 12 sec |
| Dissolution: (Not less than 75% (Q) of the labeled amount of amlodipine is dissolved) | 96.74%<br>**(Assay:** 100.34%) |

**Table 5:** Evaluation of physical and analytical parameters of formulations

| *Parameters* | *F1* | *F2* | *F3* | *F4* | *F5* | *F6* | *F7* | *F8* | *F9* |
|---|---|---|---|---|---|---|---|---|---|
| Average weight per tablet (mg) | 207 | 206 | 210 | 204 | 205 | 203 | 205 | 206 | 203 |
| Thickness (mm) | 4.55 | 4.50 | 4.52 | 4.6 | 4.58 | 4.48 | 4.55 | 4.54 | 4.55 |
| Disintegration time (sec) | 110 | 125 | 128 | 13 | 103 | 140 | 135 | 130 | 110 |
| Dissolution (%) | 102.05 | 96.70 | 95.33 | 97.27 | 98.52 | 94.04 | 88.75 | 97.75 | 99.50 |
| Assay (%) | 102.93 | 99.10 | 100.13 | 100.22 | 100.09 | 99.10 | 100.13 | 100.22 | 100.31 |

**Table 6:** Post-compression parameters of directly compressed amlodipine besylate floating tablet

| *Batch* | *Weight variation (mg)* | *Hardness Kg/cm²* | *Thickness (mm)* | *Diameter (mm)* | *Friability (%)* | *Content uniformity (%)* |
|---|---|---|---|---|---|---|
| F1 | 209 ± 6 | 6.1 ± 0.1 | 4.2 ± 0.1 | 7.6 ± 0.1 | 0.63 | 97.08 |
| F2 | 208 ± 7 | 6.0 ± 0.2 | 4.1 ± 0.1 | 7.6 ± 0.1 | 0.67 | 95.21 |
| F3 | 207 ± 8 | 6.0 ± 0.2 | 4.1 ± 0.2 | 7.7 ± 0.1 | 0.68 | 95.93 |
| F4 | 215 ± 6 | 6.4 ± 0.1 | 4.4 ± 0.1 | 7.6 ± 0.1 | 0.49 | 96.83 |
| F5 | 214 ± 5 | 6.3 ± 0.1 | 4.4 ± 0.1 | 7.6 ± 0.1 | 0.54 | 98.47 |
| F6 | 213 ± 7 | 6.2 ± 0.2 | 4.3 ± 0.1 | 7.6 ± 0.1 | 0.59 | 94.87 |
| F7 | 221 ± 6 | 6.8 ± 0.1 | 4.7 ± 0.1 | 7.6 ± 0.1 | 0.34 | 97.23 |
| F8 | 220 ± 7 | 6.6 ± 0.2 | 4.7 ± 0.1 | 7.6 ± 0.1 | 0.41 | 94.72 |
| F9 | 219 ± 6 | 6.5 ± 0.1 | 4.6 ± 0.1 | 7.6 ± 0.1 | 0.46 | 98.89 |

Weight Variation, n=20; Thickness, n=6; Hardness, n=6; Diameter, n=6

## Evaluation of Formulation

Amlosafe tablet showed parameter description as shown in Table 4.

## Evaluation of Formulation

The physical and analytical parameters of all parameters are described in Table 5 was observed. Post compression

**Table 7:** Buoyancy lag time, total floating time of formulations

| *Formulation* | *Buoyancy lag time (Sec)* | *Total floating time (Hrs)* |
|---|---|---|
| F1 | 109 | >11 |
| F2 | 107 | >11 |
| F3 | 108 | >10 |
| F4 | 120 | >11 |
| F5 | 111 | >12 |
| F6 | 109 | >10 |
| F7 | 137 | >11 |
| F8 | 131 | >10 |
| F9 | 126 | >11 |

parameters (Table 6), Buoyancy lag time and total floating time (Table 7) and cumulative %Drug release (Table 8) was observed for different formulations. The long-term and accelerated physical and analytical stability study of F9 formulation is shown in Table 9.

**Stability Study**

All physical and analytical stability parameter results of three months long term and an accelerated study found satisfactory, as given in Table 9.

***In vivo* Bioavailability Study of Amlodipine in the Formulation F9**

The plasma profiles of the drug in male Wistar rats following

**Table 8:** Cumulative % drug release of amlodipine besylate floating tablets

| *Time (hrs.)* | *F1* | *F2* | *F3* | *F4* | *F5* | *F6* | *F7* | *F8* | *F9* |
|---|---|---|---|---|---|---|---|---|---|
| 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | **0** |
| 1 | 26.41 ± 0.8 | 24.91 ± 1.1 | 26.11 ± 0.9 | 24.15 ± 0.9 | 24.01 ± 1.0 | 20.54 ± 0.9 | 21.54 ± 0.8 | 24.11 ± 1.1 | 23.57 ± 1.1 |
| 2 | 39.51 ± 0.9 | 34.12 ± 1.0 | 32.83 ± 0.7 | 32.26 ± 0.8 | 32.83 ± 1.3 | 28.11 ± 0.8 | 29.52 ± 0.9 | 35.18 ± 1.0 | 32.89 ± 0.9 |
| 3 | 48.81 ± 1.0 | 38.86 ± 0.9 | 38.11 ± 1.1 | 39.62 ± 0.6 | 39.49 ± 0.8 | 33.67 ± 0.7 | 37.77 ± 1.1 | 43.44 ± 0.9 | 40.41 ± 1.0 |
| 4 | 56.92 ± 0.9 | 49.46 ± 1.0 | 46.53 ± 0.8 | 47.54 ± 1.2 | 48.04 ± 0.7 | 39.22 ± 0.9 | 44.56 ± 0.7 | 51.52 ± 0.8 | 47.88 ± 1.1 |
| 5 | 66.21 ± 1.1 | 62.79 ± 1.3 | 56.12 ± 0.9 | 56.08 ± 0.8 | 56.67 ± 1.1 | 45.74 ± 1.0 | 53.89 ± 1.1 | 60.83 ± 1.6 | 55.65 ± 0.9 |
| 6 | 74.89 ± 0.9 | 70.82 ± 1.4 | 65.11 ± 1.1 | 64.04 ± 1.3 | 63.79 ± 0.9 | 51.12 ± 0.8 | 59.78 ± 0.9 | 69.85 ± 1.8 | 62.98 ± 1.0 |
| 7 | 81.67 ± 1.4 | 77.12 ± 1.2 | 77.08 ± 0.7 | 72.46 ± 1.0 | 71.03 ± 0.8 | 57.18 ± 0.9 | 65.96 ± 0.7 | 80.09 ± 1.1 | 69.09 ± 0.8 |
| 8 | 91.07 ± 0.8 | 82.16 ± 0.9 | 83.61 ± 0.9 | 80.81 ± 1.2 | 75.47 ± 0.8 | 66.58 ± 0.8 | 70.19 ± 1.0 | 86.19 ± 1.3 | 75.58 ± 0.9 |
| 9 | 92.54 ± 0.9 | 87.13 ± 0.7 | 88.21 ± 0.7 | 86.44 ± 1.4 | 79.97 ± 1.0 | 71.49 ± 1.1 | 75.56 ± 1.1 | 92.84 ± 0.9 | 86.29 ± 1.4 |
| 10 | 94.63 ± 1.7 | 91.04 ± 1.3 | 92.95 ± 0.9 | 91.22 ± 0.9 | 84.89 ± 1.2 | 76.89 ± 0.8 | 81.14 ± 0.9 | 94.55 ± 0.8 | 94.63 ± 1.2 |
| 11 | -- | 93.99 ± 0.9 | -- | 96.00 ± 0.8 | 88.91 ± 1.0 | -- | 87.43 ± 0.8 | -- | 96.99 ± 0.9 |
| 12 | -- | -- | -- | -- | -- | -- | -- | -- | 98.76 ± 1.1 |

**Table 9:** Physical and analytical stability study of F9 formulation

| | | | *3 Months* | | *6 Months* | |
|---|---|---|---|---|---|---|
| *Sr. No.* | *Parameters* | *Specification* | *Long term $30^0$C/65%RH* | *Accelerated $40^0$C/75% RH* | *Long term 30°C/65%RH* | *Accelerated 40°C/75%RH* |
| 1. | Description | White to off-white circular, flat beveled edged, uncoated tablets, with break line on one side and plane on other side. | Complies | Complies | Complies | Complies |
| 2. | Average weight per Tablet | 205.0 mg ± 7.5% (180 mg to 220 mg) | 203.13 mg | 203.47 mg | 203.43 mg | 203.13 mg |
| 3. | Thickness | 4.55 mm ± 0.2 mm | 4.55 mm | 4.55 mm | 4.55 mm | 4.55 m |
| 4. | Disintegration Time | Not more than 15 minutes. | 115 sec | 120 sec | 125 sec | 123 sec |
| 5. | Dissolution | Not less than 75% (Q) of the labeled amount of Amlodipine ($C_{20}H_{25}N_2O_5Cl$) is dissolved. | 102.25% | 101.58% | 97.43% | 96.16% |
| 6. | Assay | 90.0 % - 110.0 % of the labeled amount of Amlodipine | 97.43% | 95.43% | 97.73% | 95.16% |
| 7. | Total Bacterial Count | Not more than 1000 cfu/g | <10 cfu/g | <10 cfu/g | <10 cfu/g | <10 cfu/g |
| | Total Yeast & Mould Count | Not more than 100 cfu/g | <10 cfu/g | <10 cfu/g | <10 cfu/g | <10 cfu/g |
| | *E. Coli* | Absent/g | Absent/g | Absent/g | Absent/g | Absent/g |
| | *Salmonella* | Absent/10g | Absent/10g | Absent/10g | Absent/10g | Absent/10g |
| | *S.aureus* | Absent/g | Absent/g | Absent/g | Absent/g | Absent/g |
| | *P.aeruginosa* | Absent/g | Absent/g | Absent/g | Absent/g | Absent/g |

**Table 10:** Plasma concentration of Amlodipine Formulation (F9) and marketed drug

| *Time Points (Hrs)* | *Plasma Concentration (ng/mL)* | |
|---|---|---|
| | *Marketed Drug* | *Formulation F9* |
| 0 | 0 | 0 |
| 0.25 | 1.22 | 8.88 |
| 0.5 | 1.55 | 12.01 |
| 1 | 1.66 | 17.11 |
| 2 | 18.91 | 22.98 |
| 4 | 15.58 | 17.65 |
| 6 | 11.43 | 13.58 |
| 8 | 8.27 | 9.52 |
| 12 | 4.17 | 7.45 |
| 24 | 2.06 | 3.15 |
| 48 | 0.02 | 0.80 |

oral administration of the formulation (F9) and marketed tablets were compared, as shown in Table 10.

## DISCUSSION

Excipients were found suitable for floating drug delivery from tablets. Magnesium silicate, purified talc are lubricant, and Aerosil as glidant were added. Sodium bicarbonate and citric acid as standard chemicals act for the effervescence of the tablet. The major contribution of polymers HPMC and Eudragit grades was studied to release the drug from the formulation.

The ingredients do not show any physical and chemical incompatibility with the drug and, hence, be used for further study.

Use of non-complex and pharmaceutically well-presented process in developing Amlodipine Besylate floating tablets using excipients allows an integrated knowledge to deliver reliable product functionalities. Based on the product development strategy, series of experiments were conducted at the development scale. During the developmental trials, the influence of the varying manufacturing parameters on the formulation and process were investigated to verify the previously identified process parameters with the greatest impact on quality. This comprised knowledge on the variability with respect to physiochemical and functional properties in all excipients used in the formulation design. Different trial formulations are described in Table 3 to prepare different formulations containing 10 mg of amlodipine. In the development of floating tablets, citric acid and sodium bicarbonate are functioning ingredients for the release of drugs in acidic gastric medium. The composition of these ingredients was choosed according to the literature. Key changes in formulation excipients we have made were a composition of eudragit, HMPC, carbopol, and MCC. Various combinations of these ingredients with 15, 30, and 45 mg were taken and studied the effect of these polymers on an effective formulation.

'Amlosafe' tablet showed average weight of 232.0 mg with 4.0 mm thickness. 96.74% drug in marketed formulation having disintegration time 12 seconds was found.

Each of around fifty tablets were prepared of nine formulation trials and evaluated. There are changes in all parameters listed in Table 5 was observed. Based on evaluation parameters, including post-compression parameter, buoyancy lag time, total floating time, and cumulative % drug release of different formulations, the formulation F9 was selected as the best formulation. Formulation trial IXth (F9) was found satisfactory amongst the trials compared with marketed formulations.

All physical and analytical parameters of trial IX (F9 formulation) in stability study are satisfactory as shown in Table 9. Hence, the formulation F9 from trial batches was considered as prototype freeze formula containing 13.87 mg of Amlodipine Besylate USP equivalent to 10 mg of amlodipine, and total weight of formulation is compensated with an excipient.

The in vivo bioavailability study to analyze amlodipine in the formulation after oral administration was carried out A quantitative assessment of the drug was carried out in animal blood plasma.[21,22] The plasma concentration profile of the drug in F9 represents a significantly greater improvement of drug absorption than the marketed formulation as shown in Table 10.

## CONCLUSION

Floating tablets of Amlodipine besylate were developed to get optimum tablet properties and drug content. Formulation F9 containing Eudragit, HPMC polymers with carbopol and MCC in given composition were found optimized developed formulation. The in-vivo studies revealed a significantly greater extent of absorption of stable formulation than marketed tablet formulation was developed. The absorption of amlodipine from formulation resulted in multi fold increase in bioavailability as compared to marketed tablet. Our study signifies the formulation composition and its plasma concentration in rats. This can be used as oral floating tablet formulation for the patients as well can be formulated as capsule as unit dosage form.

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