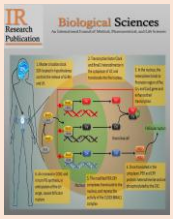
RESEARCH ARTICLE

IR Research Publication

Biological Sciences

(An International Journal of Medical, Pharmaceutical, and Life Sciences)

Journal home: https://irrespub.com/biolsciences/index.php/1/index



Development of Immediate-Release Amlodipine Tablets with Buoyancy for Improved Oral Delivery

Srividya B[1]*, Shalini P[2]

[1]*Department of Pharmaceutical Sciences and Technology, Birla Institute of Technology, Mesra-835215, India*
[2]*RITEE College of Pharmacy, Raipur-492001, India*

ARTICLE HISTORY

Received: 01-02-2023
Revised: 15-03-2023
Accepted: 17-03-2023
Online: 20-03-2023

KEYWORDS

Amlodipine
HPMC K 15M
HPMC K 100M
Carbopol 934
Immediate release floating drug delivery

ABSTRACT

This study aimed to formulate floating tablets of amlodipine using different grades of HPMC polymers with varied concentrations by direct compression method. Six formulations were prepared and evaluated for various parameters such as angle of repose, bulk density, tapped density, Carr's compressibility index, and Hausner's ratio. Tablets were subjected to several tests to determine drug content uniformity, disintegration times, floating behavior, tablet thickness, hardness, friability, weight variation, and in vitro dissolution. The optimum formulation was also evaluated for differential scanning calorimetry tests and particle size and morphology analysis. The results suggest that the direct compression method can be used to prepare floating tablets of amlodipine with suitable characteristics for oral administration.

Introduction

In recent years, hypertension has become a major public health issue worldwide, with the prevalence of high blood pressure increasing significantly. Antihypertensive medications are a group of compounds that have been developed to prevent, regulate, or treat hypertension. Among these, calcium channel blockers like amlodipine are commonly used in the treatment of heart diseases like angina and hypertension, owing to their ability to slowly and steadily adhere to targeted receptors and provide 24-hour blood pressure management. The oral route of administration is the most popular and effective for traditional drug delivery, and solid dosage forms provide the best protection for medications against various factors like temperature, light, oxygen, and stress. However, traditional immediate-release dosage forms do not always provide the desired therapeutic effect, especially for drugs with a short half-life or narrow therapeutic index. Hence, floating drug delivery systems have gained popularity in recent times, as they offer several advantages like slow and sustained drug release, improved bioavailability, and reduced dosing frequency. Polymers play a crucial role in modulating drug release in these systems, and effervescing substances like sodium bicarbonate and citric acid are sometimes added to increase buoyancy. In this study, the authors aimed to formulate a floating tablet of amlodipine using different concentrations of the polymers, by direct compression method. The pre-compressed mixtures were evaluated for various parameters, and the tablets were subjected to several tests to determine drug content uniformity, disintegration times, floating behavior, tablet thickness, hardness, friability, weight variation, and in vitro dissolution.

*Address for correspondence
Department of Pharmaceutical Sciences and Technology, Birla Institute of Technology, Mesra-835215, India.
Email: bsrividya1989@gmail.com
DOI: https://doi.org/10.55006/biolsciences.2023.03014
Published by IR Research Publication;

The optimum formulation was also evaluated for differential scanning calorimetry tests and particle size and morphology analysis. Overall, the study provides valuable insights into the formulation and evaluation of amlodipine floating tablets, which could potentially improve patient compliance and treatment outcomes in hypertensive individuals.

In the present investigation, Amlodipine was selected as a model drug for the development of floating drug delivery systems. Amlodipine is a blood pressure medication that also relieves chest pain. It expands blood vessels, which lowers blood pressure. It improves blood flow to the heart muscle, which helps to relieve angina pain. To treat hypertension and coronary artery disease, it can be used alone or in combination with other drugs. Amlodipine can be taken by adults and children aged 6 to 17 (Gradman et al.2010).

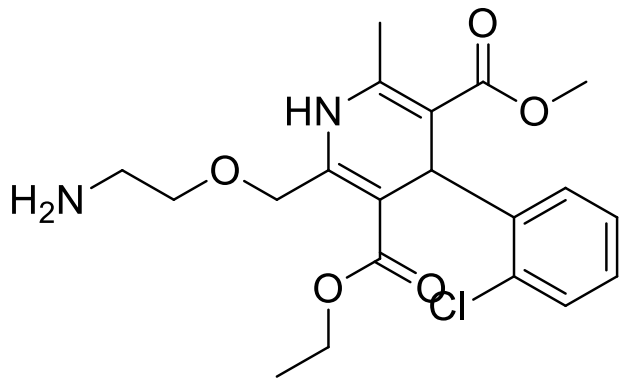


Fig.1. Structure of Amlodipine

Amlodipine having a half-life of 30-35hrs is a dihydropyridine calcium antagonist that stops calcium ions from passing across the membrane into vascular smooth muscle and cardiac muscle. Extracellular calcium ions must enter cardiac muscle and vascular smooth muscle cells through specific ion channels for them to contract. Within the physiologic pH range, amlodipine is ionized and its kinetic interaction with the calcium channel receptor is characterized by a sluggish rate of association and dissociation with the receptor binding site, resulting in a slow onset of effect. (Anon n.d.; Tripathi 2003). After oral administration of therapeutic doses, amlodipine is well absorbed with peak blood levels between 6- 12 hours post-dose. Absolute bioavailability has been estimated to be between 60 and 80%. In-vitro studies have shown that approximately 97.5% of circulating amlodipine is bound to plasma proteins and is extensively metabolized by the liver to inactive metabolites. About 10% of the parent compound and 60% of metabolites are excreted in the urine.

Materials and methods

Materials

Amlodipine, sodium bicarbonate, magnesium stearate, MCC, Carbopol 934P, talc hydroxypropyl methyl cellulose K100M, hydroxypropyl methyl cellulose K15M, citric acid, Aerosil, Poly-vinyl Pyrrolidine K30.

Preparation of floating tablets

Floating tablets containing Amlodipine were prepared by direct compression technique using varying concentrations of different grades of HPMC polymers with sodium bicarbonate and citric acid. All of the components were precisely weighed and sieved using different mesh sizes. Then, except for Magnesium stearate, all other materials were evenly combined in a glass mortar. Magnesium stearate and purified talc (1% w/w) were added after adequate mixing of the medication and other components, and the mixture was stirred for another 2-3 minutes before being crushed using a single-punch tablet machine. For all formulations, the tablet weights were kept constant.

Characterization of floating amlodipine tablets

Preformulation parameters

The quality of tablets, once formulated by rule, is generally dictated by the quality of the physicochemical properties of blends. There are many formulations and process variables involved in mixing and all of these can affect the characteristics of the blends produced. The various characteristics of blends were tested as per Pharmacopoeia.

Solubility Profile

Amlodipine solubility profile determination. The selected drug's solubility profile was determined. Water is slightly soluble, methanol is freely soluble, and ethanol is sparingly soluble.

Angle of repose

The mixture has been gently poured loose powder can be calculated using the angle through the funnel until the conical pile's peak of repose and the maximum angle that the powder just touches the funnel's tip. The radius (r) of the pile's surface with the horizontal base of the conical pile was measured.

$\text{Tan } \theta = h / r$

Table 1. Composition of all the formulations (F1–F6)

Ingredients	Batch F1	Batch F2	Batch F3	Batch F4	Batch F5	Batch F6
Amlodipine	10	10	10	10	10	10
Aerosil	5	5	5	5	5	5
Talc	5	5	5	5	5	5
Magnesium Stearate	10	10	10	10	10	10
Polyvinyl Pyrrolidine K30	10	10	10	10	10	10
Citric Acid	30	30	30	30	30	30
Sodium Bicarbonate	60	60	60	60	60	60
MCC	50	50	50	70	50	60
Carbopol 934P	70	50	50	50	60	50
HPMC K15M	50	70	50	50	60	60
HPMC K100M	50	50	70	50	50	50
TOTAL WEIGHT	350	350	350	350	350	350

Table 2. Angle of Repose values (as per USP)

The angle of repose (θ)	Nature of flow
<25	Excellent
25-30	Good
30-40	Passable
>40	Very poor

Tan θ = Angle of repose h = Height of the cone, determine the angle of repose. On a level r = Radius of the cone base. On a horizontal surface, a funnel was put above graph paper with its end at a particular height.

Bulk density

Density is defined as weight per unit volume. Bulk density is defined as the mass of the powder divided by the bulk volume and is expressed as gm/cm3. The bulk density of a powder is determined largely by particle size distribution, particle shape, and particle adhesion. Bulk density has a big impact on the size of containers needed for raw material and mix handling, shipping, and storage. It's also crucial in size mixing machines. (Rahim, Carter, and Elkordy 2015). The bulk density was calculated using the formula:

Bulk Density = M / Vo

Where,

M = weight of a sample Vo = apparent volume of powder

Tapped density

Following the procedure for measuring bulk density, the cylinder containing the sample was tapped with a suitable mechanical tapped density tester capable of producing 100 drops per minute, and the procedure was repeated until the difference between successive measurements was less than 2%, and the tapped volume, V, was measured to the nearest graduated unit. Using the formula, the tapped density in grams per L was obtained (Anepu, Duppala, and Sundari2017).

Tap = M / V Where Tap= Tapped Density M = Weight of sample V= Tapped volume of powder

Measures of powder compressibility

The Compressibility Index (Carr's Index) is a measure of the propensity of a powder to be compressed. It is determined from the bulk and tapped densities. In theory, the less compressible a material the more flowable it is. It is a measure of the relative importance of inter-particulate interactions as such. Such interactions are less important in a free-flowing powder, and the bulk and tapped densities will be closer in value. There are usually more interparticle interactions in poorer moving materials, resulting in a larger gap between bulk and tapped densities. The Compressibility Index, which is determined using the methods below, reflects these variations (Damodharan et al.2010).

Hausner ratio

Hausner's ratio can be determined as the ratio of tapped density to the bulk density of the powders and as the resulting equation (Jagdale et al. 2009; Shahi et al.2014).

Hausner ratio = tapped density/bulk density

Post-compression parameters

General Appearance

Table 3. Carr's index value (as per USP).

Carr's index	Properties
5 – 15	Excellent
12 – 16	Good
18 – 21	Fair to Passable
2 – 35	Poor
33 – 38	Very Poor
>40	Very-very poor

The general appearance of tablets, visual identity, and overall elegance is essential for consumer acceptance, control of lot-to-lot uniformity and general tablet uniformity, and monitoring the production process. The control of general appearance involves the measurement of attributes such as a tablet's size, shape, color, presence or absence of odor taste, surface textures, physical flaws, and consistency.

Size and Shape

The type of tooling determines the shape and the dimensions of compressed tablets during the compression process. Tablet thickness varies with changes in die fill, particle size distribution, and packing of the powder mix being compressed, as well as tablet weight, at constant compressive pressure, while thickness varies with variation in compressive load at a constant die fill. Only if the tablet granulation or powder mix is suitably uniform in particle size and particle size distribution, if the punch tooling is of consistent length, and if the tablet press is clean and in excellent operating order will tablet thickness be consistent from batch-to-batch or within a batch.

Tablet thickness

The thickness of the tablet was set using a Vernier caliper. The average results were determined using twenty floating tablets. When it comes to recreating the look, tablet thickness is important. When it comes to reproducing appearance, tablet thickness is important. The average thickness of the core and coated tablets is determined, and the variance is shown (Jagdale et al.2009).

Hardness test

The hardness of a tablet is defined as the force applied across the diameter of the tablet to break the tablet. The hardness of the tablet determines its resistance to chipping, abrasion, or breaking during storage transformation and handling before use. The hardness of three tablets was measured using a Monsanto hardness tester for each formulation, and the average was computed and reported with deviation (Alhamdany and Abbas 2018; Damodharan et al. 2010)

Friability

It is measured by the mechanical strength of tablets. Roche friabilator was used gold-palladium by using Sputter Coater, after fixing the sample in individual stabs to determine the friability. Pre-weighed tablets 20 tablets were placed in the friabilator. The tablets were rotated at 25 rpm for 4 minutes (100 rotations), and the tablets were then dusted and reweighed. Tablets that lose no more than 1% of their weight are typically deemed to be acceptable. The following equation was used to compute percentage friability. (Cifuentes et al. 2013; El-Bagory et al. 2012; Pawar et al. 2013).

$$\% \text{ Friability} = [(W1-W2) / W] \times 100$$

Where

W1 = Initial weight of four tablets

W2 = Weight of the four tablets after testing

Weight variation

To study the weight variation, twenty tablets were taken, and their weight was determined individually and collectively on a digital weighing balance. The average weight of one tablet was determined from the collective weight. If the weights of not more than 2 of the floating tablets differ from the average weight by more than the percentage indicated in the USP, and no tablet differs in weight by more than double that percentage, the standards are followed (Ashok and Damodar 2013; Chowdhury 2012). The percent deviation was calculated using the following formula.

% Deviation = (Individual weight – Average weight / Average weight) ×100 pharmacopeial specifications for tablet weight variation.

Disintegration Time

The test is carried out on the 3 tablets using the apparatus specified in USP, distilled water at 37 0C ± 2 0C was used as a disintegration media, and the time in seconds taken for complete disintegration of

the tablet with no palpable mass remaining in the apparatus was measured in seconds.

Particle size and Morphology analysis (SEM)

The particle size of micro-particles was determined using the optical microscopy method. Approximately 100 micro-particles were counted for particle size using a calibrated optical microscope Surface morphology of the microsphere was determined by Scanning Electron Microscope (SEM).

Differential scanning calorimetry (DSC)

The possibility of drug-excipient interaction was further investigated by differential scanning calorimetry. DSC curve for each pure powder of amlodipine, hydroxypropyl methylcellulose (HPMC) K15M, K100M, in addition to the physical mixture of the optimum formula of amlodipine in the presence of polymers (Precompression) and compressed tablet (post-compression) analysis was implemented using DSC instrument. The samples were accurately weighed and heated in a sealed aluminum pan at a rate of 10 °C/min. within a 10 and 250 °C temperature range under a nitrogen flow of 40 ml/min (Pawar and Dhavale2014).

In vitro Buoyancy studies

These studies can be performed by taking tablets (n = 3) and place in 1000 ml of 0.01 N HCl in a USP type II dissolution apparatus (37±0.5 °C, 50 rpm). The time desired for tablets to float at the topmost of the medium was considered as floating lag time. The interval of time the tablet continuously kept on the surface was considered the total floating time (Biswas et al. 2002; Sungthongjeen, Sriamornsak, and Puttipipatkhachorn 2011). Formula indicated that floating tablets made with a greater viscosity grade of hydroxypropyl methylcellulose (HPMC) K100M had a longer floating lag time and total floatation duration of more than 24 hours than those made with a lower viscosity grade of hydroxypropyl methylcellulose (HPMC) K15M. It was most likely due to increased polymer entanglement and gel strength, as well as a reduced effective molecular diffusion area inside a high viscosity hydroxypropyl methylcellulose grade compared to a low viscosity grade (HPMC) (Patel, Patel, and Jogani 2007). The level of CO2 produced is proportional to the amount of sodium bicarbonate (NaHCO3) in the tablet. The availability of a greater quantity of CO2 when the concentration of sodium bicarbonate (NaHCO3) was raised, being caught in the produced gel to give buoyancy, can be attributed to the decrease in a floating lag time of the formulations (Meka et al. 2008; Vanitha, Varma, and Ramesh2013).

In vitro dissolution studies

USP-II Paddle apparatus, Dissolution Medium 0.1 N HCl, RPM – 50, Sampling intervals (hrs) - 0.5,1,2,3,4,5,6. Temperature - 37°C±0.5°C. As the preparation was for floating drug release given through the oral route of administration, different receptors fluids are used for evaluating the dissolution profile. The release of amlodipine from floating tablets was executed by USP Dissolution Test Apparatus Type- II (Paddle method; Copley-USA). The temperature of the dissolution medium (0.1 N HCl, 900 ml) was maintained at 37±1 ˚C with a stirring rate of 50 rpm. The floating tablets were dropped inside the dissolution apparatus vessels. A 5 ml sample of the solution was withdrawn hourly, and the same number of samples was replaced with a fresh dissolution medium. The obtained samples were filtered and analyzed in a triplicate using a UV-visible spectrophotometer at 366 nm and the % drug release was calculated using an equation obtained from a standard calibration curve (Arza, Gonugunta, and Veerareddy 2009; Sucharitha et al.2013).

Results and discussion

Characterization of floating amlodipine tablets

Pre-compression parameters

Precompression parameters play a vital role in improving the flow properties of pharmaceuticals, particularly in tablet formulation. These contain an angle of repose, bulk density, tapped density, Carr's index, and Hausner ratio.

Angle of repose

Values for the angle of repose were shown in (table 4) and found to be in the range of F1-38.65, F2-30.23, F3-36.35, F4-32.10, F5-33.56, F6-35.46 indicating good flow properties.

Bulk density

Values for the bulk density that were shown in (table 4) are found to be in the range of F1-0.46, F2-0.49, F3-0.52, F4-0.43, F5- 0.45, F6-0.48.

Tapped density

Table 4. Pre-compression parameters.

Formulations	Angle of repose	Bulk density (gm/cm2)	Tapped density (gm/cm2)	Compressibility index	Hausner's ratio
F1	38.65	0.46	0.52	14.29	1.13
F2	30.23	0.49	0.51	12.35	1.04
F3	36.35	0.52	0.45	13.18	1.15
F4	32.10	0.43	0.51	13.26	1.18
F5	33.56	0.45	0.48	12.45	1.09
F6	35.46	0.48	0.46	13.35	1.11

Table 5. General appearance.

Description amlodipine	results
Colour	White crystalline powder
Odor	Odorless
Taste	Tasteless

Table 6. Size and Shape.

Raw material (API)	nature of sample
Amlodipine	Fine powder

Table 7. Particle size.

S.N.	Formulation code	Particle size µm
1	F1	183
2	F2	198
3	F3	249
4	F4	289
5	F5	326
6	F6	358

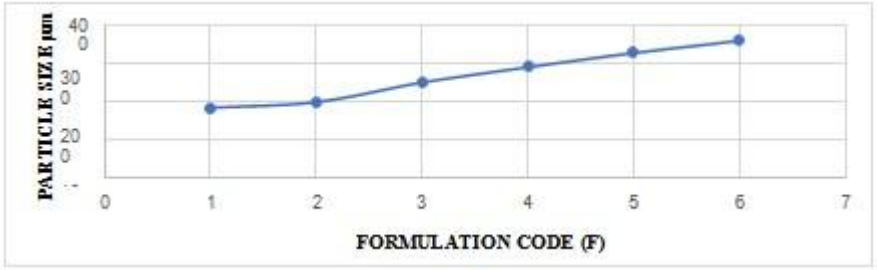


Fig 2. Particle size

Values for the Tapped density shown in (table 4) are found to be in the range of F1-0.52, F2-0.51, F3-0.45, F4- 0.51, F5-0.46, F6-0.46.

Carr's compressibility index

Carr's Index is considered a mensuration of powder bridge strength and stability. Thus, the values of the compressibility index range between F1-14.29. F2-12.35, F3-13.18, F4-13.26, F5-12.45, and F6-13.35 showed in (table 4) and this point outs the good flowability of the powder blend.

Hausner's ratio

Hausner's ratio was measured to determine the inter-particulate friction and consolidation. The powder blend of most formulas has Hausner's ratio F1-1.13, F2- 1.04, F3-1.15, F4-1.08, F5-1.09, F6-1.11 shown in (Table 4) and thus indicates good flow properties.

Post-compression parameters

Drug Content uniformity

Values for the drug content uniformity were shown in (table 9) and are found to be in the range of F1-97.01, F2-99.51, F3-98.05, F4-97.42, F5- 96.31, F6-97.46.

Tablet thickness

The thickness of the tablets was shown in (table 8) which was between (4.1±0.01-4.5±0.03 and) mm. From these results, it can be detected that those batches with a low concentration of polymer showed less thickness of the tablets obtained due to

Table 8. Drug content uniformity.

Formulation	Drug content uniformity (%)	Thickness (mm)	Hardness (kg/cm2)	Friability (%)	Weight Variation (mg)	Disintegration times (sec)
F1	97.01	4.2	4.5	0.84%	354±5%	120
F2	99.51	4.1	4.5	0.93%	353±5%	102
F3	98.05	4.3	4.3	0.85%	351±5%	110
F4	97.42	4.5	4.4	0.90%	355±5%	98
F5	96.31	4.2	4.3	0.87%	352±5%	115
F6	97.46	4.4	4.4	0.90%	353±5%	109

Table 9. Buoyancy Lag Time, Total Floating Time.

Formulation	Buoyancy Lag Time (Sec)	Total Floating Time (hrs)
F1	133 sec	>12 hrs
F2	140 sec	>20 hrs
F3	141 sec	>24 hrs
F4	110 sec	>16 hrs
F5	120 sec	>18 hrs
F6	129 sec	>22 hrs

lower concentrations of polymer. Moreover, a higher concentration of polymers produces more thickness for less dense tablets.

Hardness test

In table 8 the hardness of the tablets was between (4.3-4.5) kg/cm2 and this confirms the best characteristics of handling for all the batches.

Friability test

The friability of the tablets is normally performed and quite expectedly as shown in (table 8). The results of all formulas were in the range (0.84±0.04-0.93±0.02)

Weight variation

Weight is a compendial standard to assess the quality of tablets, and thus the weight variation test must indicate that all the tablets were uniform with low standard deviation values. The amlodipine floating tablets (tablet 8) indicates that the weight variation of all formulas was in the range of F1-354±5, F2-353±5, F3-351±5, F4-355±5, F5- 352±5, F6-353±5%.

Disintegration times

A disintegration test was conducted for all the formulations. The disintegration times of amlodipine containing HPMC K15M, and HPMCK100M was in the increasing order of effectiveness of super disintegrants with respective to the disintegration time in amlodipine, and was found to be F1-120 sec, F2102 sec, F3-110 sec, F4-98 sec, F5-115 sec, F6-109 sec.

Particle size and morphology analysis (SEM)

When analyzing the size and morphology of particles through SEM while keeping the drug ratio constant and varying the polymer ratio, an increase in polymer concentration leads to an increase in viscosity. This increase in viscosity affects the interaction between the dispersed phase and dispersion medium, which in turn influences the size concentration of particles. As a result of this, the relative viscosity and mean particle size also increase. The drug-loaded batches had a particle size ranging from 183 to 358 μm, as shown in Table 7 which lists the mean particle size for all the formulations along with their standard deviation and the number of determinations (n=3).

Differential scanning calorimetry (DSC)

The physical mixture showed no shift in the melting endotherm for amlodipine besylate but gave a broad endotherm indicating that there is no chemical interaction between the amlodipine besylate and mixture of polymers (HPMC K15M and K100M) nonetheless depicted some miscibility of the drug with polymers. The DSC thermogram of the optimized formula depicted a similar melting point as observed with the pure amlodipine powder. DSC thermogram of the optimized formulation also shows some step changes in the heat curve. These step changes are glass transition temperature which indicates the amorphous nature of other components of formulation like hydroxypropyl methylcellulose (HPMC) K15M, K100M (Choudhari et al. 2018; Damodharan et al. 2010; Govindasamy, Krishnamoorthy, and Rajappan 2013; Vora et al.2016).

In vitro Buoyancy studies

Table 10. Cumulative drug release.

Time (hrs)	Formulation 1	Formulation 2	Formulation 3	Formulation 4	Formulation 5	Formulation 6
0.5	16.2	14.6	26.4	13.4	20.3	15.8
1.0	21.5	26.9	31.3	22.6	26.4	29.4
2.0	43.9	40.1	44.1	34.3	39.8	37.5
3.0	54.6	55.3	58.9	49.5	41.3	52.1
4.0	65.7	64.8	69.5	58.1	50.1	67.3
5.0	71.1	70.5	85.2	66.4	62.6	72.4
6.0	86.4	83.0	96.6	82.6	72.6	81.8
7.0	97.6	93.1	-	91.7	87.1	86.4

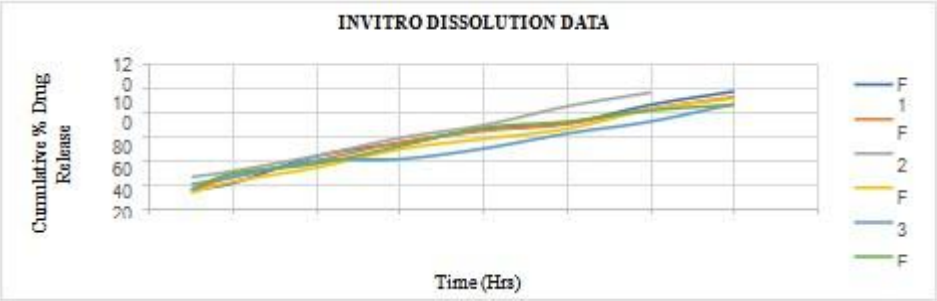


Figure 3. In vitro drug release studies dissolution parameter.

In vitro Buoyancy studies

Buoyancy lag time (BLT) and total floating time (TFT) of different formulations were noted, where F1-BLTof 133sec and TFT of >12 hours, F2 BLT of 140 sec and TFT of >20 hours, F3 BLT of 141 sec and TFT of >24 hours, F4 BLT of 110 sec and TFT of >16 hours, F5 BLT of 120 sec and TFT of >18 hours, F6 BLT of 129 sec and TFT of >22 hours About buoyancy studies results in it can be concluded that the batch containing HPMC polymers showed good buoyancy lag time (BLT) and total floating time(TFT).

The floating behavior of amlodipine tablets, including the floating lag time and total floating time, was studied and demonstrated in this study (Table 10). These floating tablets were all coated with different grades of hydrophilic polymers.

Floating behavior of tablets well as hydrophobic polymers, and then tested for CO2 bubble entrapment effectiveness and matrix integrity. Floating tablets (F1-F6) made with hydroxypropyl methylcellulose (HPMC) K15M, K100M [hydrocolloid gelling agent] absorb water and swell when they come into contact with an aqueous media (0.1 N HCl, pH 1.2), delaying medication release. In addition, the floating property of these produced tablets was tested to see how raising the hydroxypropyl methylcellulose (HPMC) K15M, and K100M concentrations affected the floating property. This polymer was discovered to be capable of maintaining matrix integrity for an extended period, with a reduction in floating lag time and a total floatation time of more than 24 hours. This might be explained by the fact that when the volume increased faster than the mass increased during swelling, the density decreased and the systems started to float.

In vitro dissolution studies

It was evident that formulations (F1-F6) showed rapid release within 7 h, Formulations (F1 and F6) were chosen to determine the effect of sodium bicarbonate (NaHCO3) concentration on drug release. As shown in Table 10, raising the concentration of different formulations F1 to F6, sodium bicarbonate had no statistically significant effect ($p>0.05$) on the drug release rate. The impact of different methylcellulose (HPMC) grades on the solubility profile of amlodipine from formulations (F1 and F6) was investigated, as shown in Table 11. The cumulative drug release rate from hydroxypropyl methylcellulose (HPMC) K100M was substantially lower (p0.05) than that from HPMC K15M. This is attributed to a decrease in initial burst release, which might be related to increased swelling of the high-viscosity polymer as the number of swelling increases, resulting in improved matrix integrity and a longer diffusional route length. As a result, water permeability is reduced. In terms of medication release rate, it was determined by the viscosity grade and concentration of the polymers used (El Nabarawi et al.2017).

In vitro drug release studies

The study focused on in vitro dissolution of the drug and analyzed the effects of sodium bicarbonate concentration and different grades of hydroxypropyl methylcellulose (HPMC) on drug release. Formulations (F1-F6) exhibited rapid drug release within 7 hours, and F1 and F6 were selected

for further investigation. Increasing the concentration of sodium bicarbonate did not significantly affect the drug release rate. The study also found that HPMC K100M resulted in a substantially lower cumulative drug release rate compared to HPMC K15M, likely due to increased swelling of the high-viscosity polymer leading to improved matrix integrity and a longer diffusional route length. The medication release rate was determined by the viscosity grade and concentration of the polymers used. Table 11 shows the cumulative drug release rate from the formulations at different time intervals. At 0.5 hours, F3 showed the highest cumulative drug release rate at 26.4%, while F2 exhibited the lowest release rate at 14.6%.

Conclusion

This research found a single optimal amlodipine floating tablet formula (F6) that allowed for the production of effective tablets including a mix of hydrophilic and lipophilic polymers. Floating tablets of Amlodipine might be produced in the current study to improve stomach residence duration and hence bioavailability. Also, the administration frequency might be lowered. Amlodipine besylate floating tablets made with the hydrophilic controlled release polymer HPMC K100M and Carbopol were found to float for the longest period and release the medicine in a gradual and controlled way. The percentage of drug release rate depends on the percentage of polymer used. The developed system offers a simple and novel technique for a gastric retentive drug delivery system. Such work can be further extended using some other controlled-release polymers for drug delivery.

Contribution of authors

NA

Acknowledgments

NA

Conflict of interest

The authors declare that they have no conflict of interest.

References

1. Abernethy, Darrell R., and Janice B. Schwartz. Pharmacokinetics of Calcium Antagonists under Development. Clinical Pharmacokinetics. 1988;15(1):1–14.
2. Agarwal, Manyoo A., David Flatt, and Rami N. Khouzam. The Potential Detrimental Effects of Calcium Channel Blockers' Overdose and Current Available Management. Annals of Translational Medicine. 2018;6(1).
3. Alhamdany, Anas T., and Ali Khidher Abbas. Formulation and In Vitro Evaluation of Amlodipine Gastroretentive Floating Tablets Using a Combination of Hydrophilic and Hydrophobic Polymers. Int J App Pharm. 2018;10(6):126–34.
4. Anepu, Sarada, Lohithasu Duppala, and S. Sundari. Formulation Development, Characterization, and In Vitro Evaluation of Floating Matrix Dosage Form of Tramadol Hydrochloride Using Various Polymers. Asian J Pharm Clin Res. 2017;10:281–90.
5. British-National-Formulary-for-Children_-the-Risk-of-Inappropriate-Paracetamol-Prescribing. [Internet]. [cited 2023 Feb 26]. Available from: https://bnfc.nice.org.uk/news/risk-of-inappropriate-paracetamol-prescribing/
6. Arza, Ramji Anil Kumar, Chandra Sekhara Rao Gonugunta, and Prabhakar Reddy Veerareddy. Formulation and Evaluation of Swellable and Floating Gastroretentive Ciprofloxacin Hydrochloride Tablets. AAPS PharmSciTech. 2009;10(1):220–26.
7. Ashok, K. P., and K. S. Damodar. Effect of Hydrophilic and Hydrophobic Polymers and Fillers on Controlled Release Matrix Tablets of Acyclovir. Der Pharm Sinica. 2013;4:143–50.
8. Biswas, Kausik, Ishita Chattopadhyay, Ranajit K. Banerjee, and Uday Bandyopadhyay. Biological Activities and Medicinal Properties of Neem (Azadirachta Indica). Current Science. 2002;82(11):1336–45.
9. Choudhari, Prashant Kumar, H. K. Jain, P. Sharma, and B. Srivastava. A Novel Co-Processed Directly Compressible Release-Retarding Polymer: In Vitro, Solid State and in Vivo Evaluation. Future Journal of Pharmaceutical Sciences. 2018;4(1):29–40.
10. Chowdhury, M. Ehsanul H. Preparation and Evaluation of Floating Matrix Tablets of Ranitidine Hydrochloride. The Pharma Innovation. 2012;1(7).
11. Cifuentes, Celia, Angela Aguilar-de-Leyva, Ali R. Rajabi-Siahboomi, and Isidoro Caraballo. Critical Points in Ethylcellulose Matrices: Influence of the Polymer, Drug and Filler Properties. Acta Pharmaceutica. 2013;63(1):115–29.
12. Damodharan, N., V. Manimaran, and B. Sravanthi. Formulation Development and Evaluation of Delayed-Release Doxycycline Tablets. International Journal of Pharmacy and Pharmaceutical Sciences. 2010;2(Suppl
13. El-Bagory, Ibrahim, Nahla Barakat, Mohamed Ibrahim, and Fouza ElEnzi. 2012.

—Formulation and in Vitro Evaluation of Theophylline Matrix Tablets Prepared by Direct Compression: Effect of Polymer Blends.‖ Saudi Pharmaceutical Journal 20(3):229–38.
14. Elliott, William J. 2012. —NICE Clinical Guideline 127: Hypertension: Clinical Management of Primary Hypertension in Adults.‖ Yearbook of Medicine 2012:336–38.
15. Foëx, Phil, and J. W. Sear. 2004. —Hypertension: Pathophysiology and Treatment.‖ Continuing Education in Anaesthesia Critical Care & Pain 4(3):71–75.
16. Govindasamy, GOPI, KANNAN Krishnamoorthy, and MANAVALAN Rajappan. 2013. —Selection of Excipients for Nanoparticles Formulations of Nateglinide through Drug-Excipients Compatibility Study.‖ International Journal of Pharmacy and Pharmaceutical Sciences 5(2):371–77.
17. Gradman, Alan H., Jan N. Basile, Barry L. Carter, George L. Bakris, and American Society of Hypertension Writing Group. 2010. —Combination Therapy in Hypert.
18. Gupta, M. M. (2013). Formulation development and evaluation of immediate release tablet of anti-hypertensive drug olmesartan medoxomil. The Pharma Innovation, 2(3), Part A, 68.
19. Hamid, A., & Merchant, M. (2006). Harris Shoiab, Jaweria Tazeen. Once daily tablet formulation and in vitro release evaluation of cefpodoxime using HPMC. AAPS Pharm Sci Tech, 7(3).
20. Hermida, R. C., Ayala, D. E., Mojón, A., & Fernández, J. R. (2008). Chronotherapy with nifedipine GITS in hypertensive patients: improved efficacy and safety with bedtime dosing. American Journal of Hypertension, 21(8), 948–54.
21. Jagdale, S. C., Agavekar, A. J., Pandya, S. V., Kuchekar, B. S., & Chabukswar, A. R. (2009). Formulation and evaluation of gastroretentive drug delivery system of propranolol hydrochloride. AAPS PharmSciTech, 10(3), 1071–79.
22. Julius, S. (1988). Amlodipine in hypertension: an overview of the clinical dossier. Journal of Cardiovascular Pharmacology, 12, S27-33.
23. Meka, L., Kesavan, B., Chinnala, K. M., Vobalaboina, V., & Yamani, M. R. (2008). Preparation of a matrix type multiple-unit gastroretentive floating drug delivery system for captopril based on gas formation technique: in vitro evaluation. AAPS PharmSciTech, 9(2), 612–19.
24. El Nabarawi, M. A., Terima, M. H., Abd El-Monem, R. A., El Nabarawy, N. A., & Gaber, D. A. (2017). Formulation, release characteristics, and bioavailability study of gastroretentive floating matrix tablet and floating raft system of mebeverine HCl. Drug Design, Development and Therapy, 11, 1081.
25. Oparil, S., Zaman, M. A., & Calhoun, D. (2003). Pathogenesis of hypertension. Annals of Internal Medicine, 139(9), 761–76.
26. Palma-Gámiz, J. L. (1997). High blood pressure and calcium antagonism. Cardiology, 88(Suppl.1), 39–46.
27. Pare, A., Yadav, S. K., & Patil, U. K. (2008). Formulation and evaluation of effervescent floating tablet of amlodipine besylate. Research Journal of Pharmacy and Technology, 1(4), 526–30.
28. Patel, D. M., Patel, N. M., & Jogani, P. D. (2007). Formulation and optimization of carbamazepine floating tablets. Indian Journal of Pharmaceutical Sciences, 69(6), 763.
29. Pawar, H. A., & Dhavale, R. (2014). Development and evaluation of gastroretentive floating tablets of an antidepressant drug by thermoplastic granulation technique.
30. Pawar, Harshal Ashok, Pooja Ramchandra Gharat, Rachana Vivek Dhavale, Pooja Rasiklal Joshi, and Pushpita Pankajkumar Rakshit. 2013. "Development and Evaluation of Gastroretentive Floating Tablets of an Antihypertensive Drug Using Hydrogenated Cottonseed Oil." International Scholarly Research Notices 2013.
31. Rahim, Safwan Abdel, Paul A. Carter, and Amal Ali Elkordy. 2015. "Design and Evaluation of Effervescent Floating Tablets Based on Hydroxyethyl Cellulose and Sodium Alginate Using Pentoxifylline as a Model Drug." Drug Design, Development and Therapy 9:1843.
32. Reddy, K. Sai Madhav, Laxmidhar Sahoo, Dr. G. Kamalakar Reddy, and L. Vamsi Krishna. 2011. "Formulation and Evaluation of Immediate Release Tablets of Linezolid." International Journal of Pharmaceutical & Biological Archives 2(4):1230-35.
33. Shahi, Sadhana R., Shivram B. Shinde, Nityanand S. Zadbuke, and Abhay N. Padalkar. 2014. "Formulation Development and Evaluation of Floating Matrix Tablet of Verapamil HCl." Asian Journal of Pharmaceutics (AJP): Free Full-Text Articles from Asian J Pharm 7(1).
34. Sheraz, Muhammad Ali, Syed Furqan Ahsan, Marium Fatima Khan, Sofia Ahmed, and Iqbal Ahmad. 2016. "Formulations of Amlodipine: A Review." Journal of Pharmaceutics 2016.
35. Singh, Brahma N., and Kwon H. Kim. 2000. "Floating Drug Delivery Systems: An Approach to Oral Controlled Drug Delivery via Gastric Retention." Journal of Controlled Release 63(3):235-59.

36. Sinha, V. R., M. K. Agrawal, and R. Kumria. 2005. "Influence of Formulation and Excipient Variables on the Pellet Properties Prepared by Extrusion Spheronization." Current Drug Delivery 2(1):1-8.
37. Sood, Richa, M. S. Rathore, A. Sharma, Richa Thakur, J. Chaudhari, and V. Soni. 2012. "Immediate Release Antihypertensive Valsartan Oral Tablet: A Review." Journal of Scientific Research in Pharmacy May 1(2):20-26.
38. St-Onge, M., P. A. Dubé, S. Gosselin, C. Guimont, J. Godwin, P. M. Archambault, J. M. Chauny, A. J. Frenette, M. Darveau, and N. Le Sage. 2014. "Treatment for Calcium Channel Blocker Poisoning: A Systematic Review." Clinical Toxicology 52(9):926-44.
39. Sucharitha, M., A. N. Devi, V. P. Priya, and Sharma J. V. C. Shyamala. 2013. "Formulation and Evaluation of Gastroretentive Floating Tablets of Valsartan." World J Pharm Pharm Sci 3:689-702.
40. Sungthongjeen, Srisagul, Pornsak Sriamornsak, and Satit Puttipipatkhachorn. 2011. "Design of Floating HPMC.