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Research Article

# FORMULATION DEVELOPMENT AND IN-VITRO EVALUATION OF ORALLY DISINTEGRATING TABLETS OF AMLODIPINE BESYLATE

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**ABSTRACT**

An attempt has been made for the development of Orally disintegrating tablets of Amlodipine Besylate prepared by direct compression method by using super disintegrants like crosspovidone, cross caramellose sodium and sodium starch glycolate. Effect of different super disintegrants on disintegration behaviour of tablets was evaluated. All the formulations were evaluated for pre compression, post compression parameters and in-vitro dissolution. Wetting time of formulations containing crosscarmellose sodium was least and tablets showed fast disintegration. Of the nine formulations studied F9 showed short dispersion time with maximum drug realease 99.59% in 20Mins. Combinations of super disintegrants were found to be better in the formulation of fast dissolving tablets of Amlodipine Besylate rather than using alone.

**Keywords:** Amlodipine Besylate, In-Vitro Evaluation, Orally Disintegrating Tablets.

## INTRODUCTION

Recent advance in novel drug delivery system aims to enhance the safety and efficacy of the drug molecule by formulating a dosage form being for the administration[1]. Difficulty in swallowing is experienced by patient such as paediatric, geriatric, bedridden, disabled and mentally ill, including motion sickness and sudden episodes of allergic attacks, hence resulting in higher incidence of non-compliance and ineffective therapy[2]. To improve the quality of life and treatment compliances of such patients fast disintegrating or orally disintegrating tablets dosage form is a better alternative for oral medication[3]. Orally disintegrating tablets are solid dosage form containing medical substances which disintegrate rapidly, usually within few seconds when placed upon tongue requiring no additional water to facilate swallowing[4]. It is suited for tablets undergoing high first pass metabolism and is improving bioavailability with reducing dosing frequency to minimize side effect.

Fast disintegrating tablets are gaining prominence as new drug delivery systems. These dosage forms disintegrate within a minute with very less quantity of water. This can be achieved by addition of various superdisintegrants like croscaramellose sodium, crosspovidone, sodium starch glycolate alone or in various combinations. Due to the fast disintegration of dosage form, patients obtain quick pharmacological effect of active pharmaceutical ingredient [5-8].

Amlodipine is a potent calcium channel blocker. It is used to treat high blood pressure and certain types of Angina and coronary heart failure. The absolute bioavailability is approximately 65 % due to extensive hepatic metabolism[9]. Various techniques can be used to formulate orally disintegrating tablets or fast dissolving tablets[10]. Direct compression is one of the technique requires the incorporation of superdisintegrants into the formulation and use of highly water soluble excipients achieve faster tablet

disintegration.

In this study, an effort has been made to formulate orally disintegrating tablets of Amlodipine Besylate using different superdisintegrants. Objective of study was to enhance dissolution and absorption of drug, which may produce the rapid onset of action in the treatment of Hypertension.

## MATERIALS AND METHODS

Amlodipine Besylate was obtained as a gift sample from Darwin laboratories, Vijayawada.) Crosspovidone (polyplasdone xl-10, ISP, USA), Sodium starch glycolate obtained from DMV Fonterra, Netherlands. Croscaramellose sodium, gift sample from Micro Labs, Manitol obtained from Roquette, France. Spray dried lactose obtained from Meggle excipients, Germany. All chemicals and reagents used were of analytical grade.

### Preparation of orally disintegrating tablets

Amlodipine orally disintegrating tablets were prepared by direct compression method. Different concentration of excipients was used to prepare different groups of orally disintegrating tablets. Compositions of various formulations are shown in Table 1. All the ingredients of the orally disintegrating tablets of Amlodipine were weighed and mixed in mortar with the help of pestle, then finally 1.5 mg Magnesium Stearate and 3mg Aerosil was added material was slightly compressed on the 8mm flat-faced punch using a Cadmach single station tablet machine. The total weight of the formulation was maintained 150mg.

## RESULTS AND DISCUSSION

### Evaluation of orally disintegrating tablets of Amlodipine

All the batches of tablets were evaluated for various parameters like weight variation, friability, hardness, drug content, disintegration and dissolution and results reported in Table 2.

### Weight variation test[11]

Twenty tablets were taken and their weight was determined individually and collectively on a digital weighting balance. The average weight of one tablet was determined from the collective weight.

### Hardness test[12]

The hardness of the tablet was determined using Monsanto Hardness tester.

### Friability test

Six tablets from each batch were examined for friability using Roche Friabilator (Tropical Equipment Pvt. Ltd. Mumbai, India) and the equipment was run for 4min at 25 revolutions per minute. The tablets were taken out, dedusted and reweighted and % friability was calculated.

**%Friability = (Loss in weight/Initial weight) x 100**

### Wetting time[13, 14]

A piece of tissue paper folded twice was kept in a Petri dish (inter diameter 5.5cm) containing 6ml of purified water. The tablet was placed on the tissue paper and allowed to wet completely. The time required for complete wetting of the tablet was then recorded

### Drug content uniformity[15]

The drug content was determined by taking the powder equivalent to 10 mg. Then it was dissolved in 0.01 N HCl and absorbance was measured against blank at 239 nm.

### Disintegration test

The disintegration test was performed using an USP disintegration apparatus, with distilled water at 37± $2^0$C. The time reported to obtain complete disintegration of six tablets were recorded and average was reported.

### In vitro Dissolution testing

Dissolution study was conducted for all the formulation using USP Type-II apparatus (paddle type). The dissolution test was performed using 500 ml of 0.01 M HCl taken as dissolution medium at 50 rpm and 37 °C± 0.5 °C. Five millilitres of aliquots were periodically withdrawn and the sample volume was replaced with an equal volume of fresh dissolution medium. The samples were analyzed at 239nm using UV-Visible spectrophotometer.

## RESULTS

Amlodipine orally disintegrating tablets were prepared by direct compression method. The compositions of the formulations are shown in the Table1. Table 2 shows the data obtained from the evaluation of tablets. All batches of the tablets were preliminarily evaluated for various physical parameters such as hardness, friability, drug content, wetting time, disintegration and dissolution which were reported in Table no 2. All above properties and value were near to

boundary of standard limit. All the tablets maintained hardness in the range 5.0–5.1 kg/cm$^2$. The loss in total weight of the tablets due to friability was in the range of 0.21-0.31%. The drug content in different formulation was highly uniform and in the range of 97-99%. Wetting time is used as an indicator of the ease of tablet disintegration and found to be 13-28sec. The result of In-vitro disintegration were within the prescribed limits and comply with the criteria for orally disintegrating tablets, the value were with 15-33sec. In vitro dissolution studies are shown in table 3 and fig. 1, 2 and 3.

The concept of super disintegrant addition method proved to be beneficial in order to lower the disintegration time. The quicker disintegration time may be attributed to faster water uptake by the tablets. Dissolution profiles revealed that, after 20 minutes, formulations $F_1$-$F_9$ shows % Drug release of 91.71, 95.89, 97.99, 91.86, 98.03 97.96, 94.41, 98.52 and 99.59 respectively. Among all the formulations, F9 formulation shows better dissolution efficiency and rapid disintegration with release of 99.59 % within 20Min.

**Table 1: Formulation design of directly compressible Amlodipine tablets**

| INGREDIENTS (mg) | $F_1$ | $F_2$ | $F_3$ | $F_4$ | $F_5$ | $F_6$ | F7 | F8 | F9 |
|---|---|---|---|---|---|---|---|---|---|
| Amlodipine Besylate | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 |
| MCC (Avicel PH 105) | 30 | 30 | 30 | 30 | 30 | 30 | 30 | 30 | 30 |
| Mannitol | 97.25 | 93.5 | 89.75 | 97.25 | 93.5 | 89.75 | 97.25 | 93.5 | 89.75 |
| Sodium starch glycolate | 3.75 | 7.5 | 11.25 | - | - | - | - | - | - |
| Cross caramellose sodium | - | - | - | 3.75 | 7.5 | 11.25 | - | - | - |
| Cross povidone | - | - | - | - | - | - | 3.75 | 7.5 | 11.25 |
| Magnesium stearate | 1.5 | 1.5 | 1.5 | 1.5 | 1.5 | 1.5 | 1.5 | 1.5 | 1.5 |
| Aerosil | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 |
| Strawberry flavour | 1.5 | 1.5 | 1.5 | 1.5 | 1.5 | 1.5 | 1.5 | 1.5 | 1.5 |
| Aspartame | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 |

**Table 2: Evaluation parameters of tablets**

| Formulae | Hardness (kg/ $cm^2$) | Friability | Weight Variation (mg) | Drug content (%) | Disintegration time (sec) | Wetting time(sec) |
|---|---|---|---|---|---|---|
| **FI** | 5.0±0.922 | 0.22 | 150±2.20 | 98±0.88 | 33±1.00 | 28±1.23 |
| **FII** | 5.0±1.22 | 0.312 | 150±1.44 | 99±0.99 | 27±1.52 | 24±2.12 |
| **FIII** | 5.0±1.31 | 0.302 | 150±2.34 | 98±1.22 | 21±1.52 | 17±1.44 |
| **FIV** | 5.0±0.83 | 0.282 | 150±0.94 | 99±0.78 | 30±2.00 | 26±1.55 |
| **FV** | 5.0±0.68 | 0.262 | 150±0.84 | 97±1.44 | 24±2.00 | 22±2.42 |
| **FVI** | 5.0±0.96 | 0.292 | 150±1.98 | 100±0.34 | 19±1.73 | 17±1.35 |
| **FVII** | 5.0±0.98 | 0.198 | 150±1.45 | 98±1.45 | 24±2.08 | 21±2.22 |
| **FVIII** | 5.0±1.12 | 0.212 | 150±1.68 | 99±0.11 | 19±1.00 | 18±1.66 |
| **FIX** | 5.0±0.69 | 0.242 | 150±1.88 | 99±0.56 | 15±1.52 | 13±1.52 |

**Table 3: Dissolution profiles of formulations**

| Time (Min) | % Cumulative drug release | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | **F1** | **F2** | **F3** | **F4** | **F5** | **F6** | **F7** | **F8** | **F9** |
| 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 5 | 52.98 | 59.25 | 67.29 | 59.94 | 63.62 | 69.71 | 63.33 | 70.63 | 84.31 |
| 10 | 70.93 | 74.04 | 79.52 | 73.25 | 83.39 | 84.60 | 77.18 | 83.86 | 95.09 |
| 15 | 86.27 | 90.16 | 93.60 | 89.06 | 91.92 | 95.78 | 91.54 | 94.65 | 98.24 |
| 20 | 91.71 | 95.89 | 97.99 | 91.86 | 98.07 | 97.96 | 94.41 | 98.52 | 99.59 |
| 25 | 93.78 | 97.78 | 98.78 | 95.45 | 98.96 | 99.70 | 97.02 | 99.42 | 99.20 |
| 30 | 95.35 | 98.09 | 98.90 | 96.46 | 99.37 | 99.90 | 98.08 | 99.26 | 98.79 |

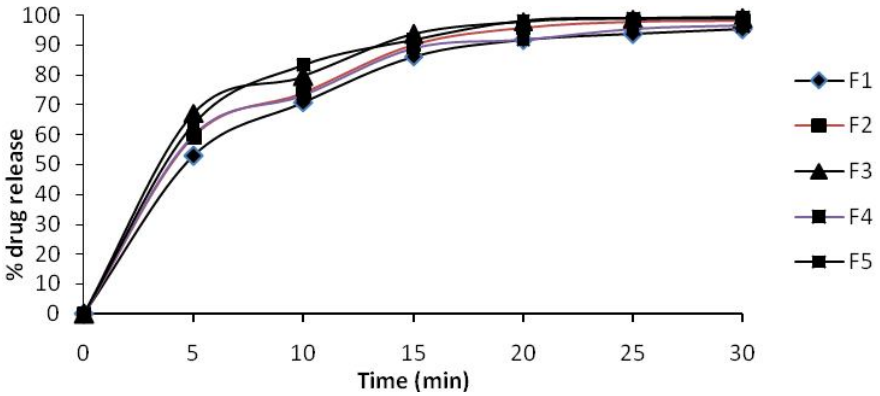


**Fig. 1: Drug release profiles of F1-F5 formulations**

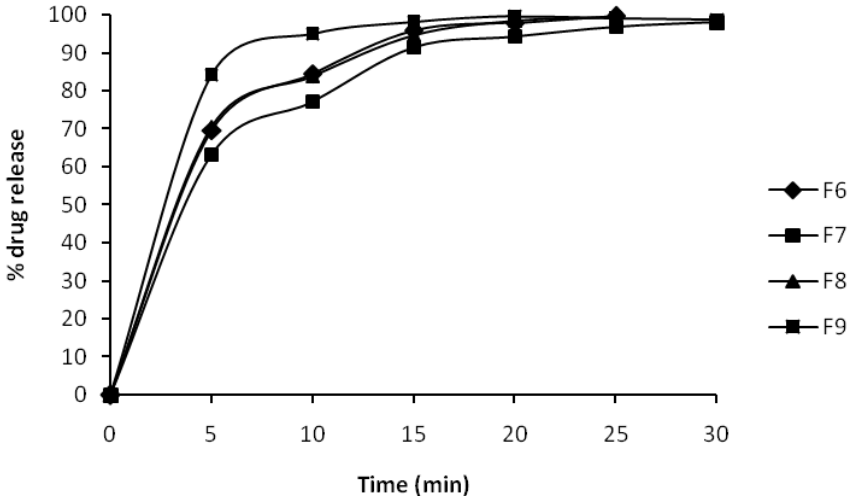


**Fig. 2: Drug release profiles of F6-F9 formulations**

## CONCLUSION

The Fast disintegrating tablets of Amlodipine Besylate were formulated by using the superdisintegrants like sodium starch glycolate, Cross caramellose sodium and Crosspovidone. The use of super disintegrant crosspovidone at concentration of 7.5% given the better release of drug when compared to other superdisinte grants. The proposed Fast disintegrating formulation possessed ideal and reproducible characteristics of disintegration time and drug release profile.

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