Academic Sciences

International Journal of Current Pharmaceutical Research

ISSN- 0975-7066 Vol 7, Issue 3, 2015

Original Article

FORMULATION AND IN-VITRO EVALUATION OF MOUTH DISSOLVING TABLETS OF AMLODIPINE AND ROSUVASTATIN

SHIREEN BEGUM, SYED ABDUL AZEEZ BASHA, SHAZIA FATIMA**

Department of Pharmaceutics, Deccan School of Pharmacy, Darussalam, Hyderabad
Email: mail2shireen@yahoo.com

Received: 05 May 2015, Revised and Accepted: 06 Jun 2015

ABSTRACT

Objective: Mouth Dissolving Tablets (MDT) are most accepted and exploited for the drug delivery for the patients who are having difficulty with swallowing i.e., mainly pediatric's and Geriatric's. Amlodipine besylate (ADB) is an anti-hypertensive and it is also used in many Coronary artery diseases, Whereas Rosuvastatin Calcium (RSC) is an anti-hyperlipidemia that prevents of Atheroma. In the present study a combination of ADB, RSC is formulated into a mouth dissolving tablet using three super disintegrants such as Croscarmellose Sodium (CCS), Cross povidone (CP), Sodium Starch Glycolate (SSG) at various concentrations to enhance the disintegration and dissolution of ADB, RSC to improve bioavailability of the drugs

Methods: The tablets were prepared by using direct compression method and evaluated for weight variations, Hardness, Friability, Wetting time, disintegration time (DT) and Dissolution study. Prepared tablets are subject to FT-IR Study for Characterization and compatibility study.

Results: No Chemical interaction between drug and excipients were indicated in the FT-IR. Disintegration and dissolution profiles decreases with addition of super disintegrating agents like Croscarmellose Sodium (CCS), Cross povidone (CP), Sodium Starch Glycolate (SSG).

Conclusion: Among all the formulation F12 with CP in 5% and SSG 5% Concentration found to be best in drug release profile.

Keywords: Mouth Dissolving Tablets, Amlodipine besylate, Rosuvastatin Calcium, super disintegrants, direct compression method.

INTRODUCTION [1, 2, 3, 4, 5, 6]

Mouth dissolving tablets are solid dosage forms containing drugs that disintegrate in the oral cavity within less than one minute leaving an easy-to-swallow residue. In the recent trend the development of mouth dissolving tablets formulation is emerging and gaining popularity because it is easy to administer and leads to better patient compliance. Mouth dissolving drug technology is one of the best and ideal methods to improve patient compliance and bio availability and to gives immediate relief. There are various conventional methods to prepare MDT in which direct compression is used in the present study. These tablets were prepared with very low compression force. In the present study Amlodipine (anti-hypertensive) and Rosuvastatin (anti-hyperlipidemia) are having low solubility in water. There solubility and their disintegration, Dissolution rate is increased by incorporating super disintegrating agent like Croscarmellose Sodium, Cross povidone, Sodium Starch Glycolate increasing concentration.

MATERIALS AND METHODS

Amlodipine besylate, Rosuvastatin Calcium were received as gift samples from Dr. reddy Lab's, Hyderabad, Sodium Starch glycolate, Crosscarmellose sodium, Microcrystalline cellulose, Cross povidone, Magnesium Stearate are obtained from commercial sources (SD fine chemicals) and all the reagents used are of analytical grade.

Methodology

Mouth dissolving tablets of Amlodipine Besylate and Rosuvastatin Calcium is prepared by geometric mixing, all the ingredients were weighed according to the formula in table No. 1 such that 3 super disintegrates are added at 3 different concentrations such a 2%, 5%, 8%. The obtained blend was then punched into tablets by following direct compression method using a single stage tablet punching machine.

Evaluation of mouth dissolving tablets of amlodipine and rosuvastatin

a. Pre compressed parameters [7-12]

Bulk Density

Blend was weighed and transferred to a measuring cylinder. Then bulk volume was noted. Bulk density was calculated by using the following formula.

$$\text{Bulk Density} = \frac{Mass\ of\ th\ Powder}{Bulk\ Volume}$$

Table 1: Formula of mouth dissolving tablet of amlodipine besylate and rosuvastatin calcium

S. No.	Name of the ingredients	Quantities in mg per one tablet											
		F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
1.	Amlodipine (mg)	10	10	10	10	10	10	10	10	10	10	10	10
2	Rosuvastatin(mg)	10	10	10	10	10	10	10	10	10	10	10	10
3	Sodium Starch Glycolate (%)	2	5	8	-	-	-	-	-	-		5	5
4	Cross Carmellose Sodium (%)	-	-	-	2	5	8	-	-	-	5	5	-
5	Crospovidone (%)	-	-	-	-	-	-	2	5	8	5	-	5
6	Mag. stearate (%)	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
7	Aerosil (%)	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
8	Citric acid (%)	1	1	1	1	1	1	1	1	1	1	1	1
9	Vanillin (%)	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2
10	Saccharin(%)	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3
11	Microcrystalline cellulose	q. s	q. s	q. s	q. s	q. s	q. s	q. s	q. s	q. s	q. s	q. s	q. s
12	TOTAL WT(mg)	150	150	150	150	150	150	150	150	150	150	150	150

Tapped density

Blend was weighed, transferred to measuring the cylinder and subjected to 500 tappings. Then volume was noted as tapped volume. Tapped density was measured by using the following formula

$$\text{Tapped Density} = \frac{Mass\ of\ the\ Powder}{Tapped\ Volume}$$

Carr's Index

Carr's index was calculated by using the following formula.

$$\text{Carr's index} = \frac{Tapped\ density - Bulk\ density}{Tapped\ density} \times 100$$

Hausner's ration

Hausner's ratio is an index of ease of powder flow; it calculated by following formula.

$$\text{Hausner's Ratio} = \frac{Tapped\ Density}{Bulk\ Density}$$

Angle of repose

Angle of Repose (θ) is the maximum angle between the surface of a pile of powder and horizontal plane. It is usually determined by Fixed Funnel Method

b. Post compression parameters: [7-12]

The prepared tablets were evaluated for weight variation, hardness, friability, Disintegration time, wetting time, drug content studies.

Weight variation

In a weight variation test twenty tablets were selected at random and average weight was calculated. Then individual tablets were weighed and the weight was compared with an average weight.

Tablet Hardness

It is done by using monsantto hardness tester. Selected tablet was placed in between the plungers and the handle was pressed, the force of fracture was recorded and the friability of the tablets was determined using Lab India friabilator and thickness was measured by using vernier calipers.

Disintegration time

The *in-vitro* disintegration time of a tablet was determined using disintegration test apparatus as per I. P. specifications. One tablet is placed in each of the 6 tubes of the basket. A Disc was added to each tube, and experiment done by using Phosphate buffer H 6.8 maintained at 37±2oC as immersion liquid. Assembly raised and lowered. The time taken for tablet to complete disintegration with no palpable mass remaining in the apparatus was measured was recorded in seconds.

Wetting time

In wetting time a piece of tissue paper folded twice was placed in small petri dish (i. d=6.5 cm) containing 10 ml of water, a tablet was placed on the paper, and the time for complete wetting was measured. Three trails for each batch were performed and standard deviation was also determined.

Drug content

10 tablets were taken and powdered. Powder equivalent to one tablet was weighed accurately and allowed to dissolve in 10 ml phosphate buffer and make up volume up to 100 ml. The solution was filtered, 1 ml of filtrate was taken in 50 ml of volumetric flask and diluted up to mark with 6.8 phosphate buffer and analysed spectrophotometrically.

***In vitro* release studies**

An *in vitro* release study was conducted by suing USP type II apparatus. Paddle speed was maintained at 50 rpm and 900 ml of 6.8 pH Phosphate buffer was used as a dissolution medium. Temperate of the dissolution medium was maintained at 37±0.5oC, a sample of dissolution medium was withdrawn for every 3 min and filtered. The absorbance of filtered solution was measured by using UV-VISIBLE spectroscopy.

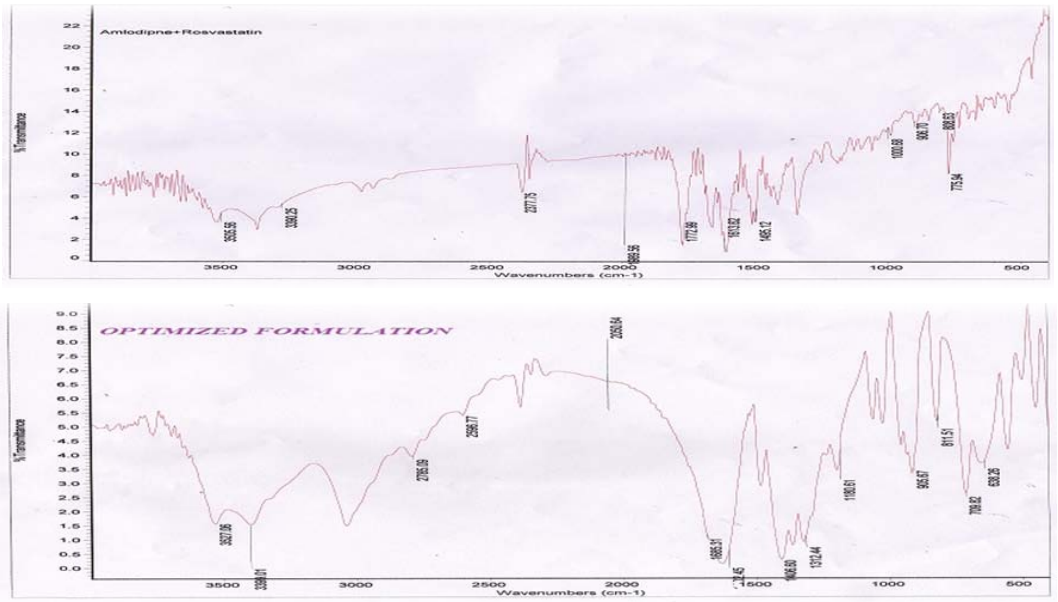

Fig. 1: FT-IR Spectrum of combined pure drug and optimized formula (12)

RESULTS AND DISCUSSION

Mouth Dissolving tablets of Amlodipine besylate and Rosuvastatin Calcium of Strength 10,10 mg were prepared by using direct compression method with three superdisintegrant such as Croscarmellose Sodium(CCS) and Cross Povidone(CP), Sodium Starch Glycolate(SSG) were used in increasing concentration as 2%,5%,8% to study the effect of concentration of Super Disintegrant on formulation Dissolution profile.

The pre compression property study were Tabulated in table 2, Hausner's Index of all the formula lies between 1.067-1.251 which is

indicate that their flow was excellent to fair which in acceptable range. Angle of repose lies between 26.61-36.54 indicating that they had had an excellent flow.

The post compression studies of Mouth dissolving tablets of Amlodipine Besylate and Rosuvastatin Calcium are tabulated in tablet 3 & table 4. They revealed that all the parameters such as Friability, Weight Variation, Hardness, Disintegration time, wetting time, drug content all are within the acceptance criteria limits for individual tests. up to Certain concentration (5%) With increase in concentration of super Disintegrant, the Disintegration Time and Wetting time of tablet was decreased. The dissolution profile of the all the 12 formulas were explained in fig.2 & fig. 3. From that formulation F12 is served as better formulation as the release the maximum of drug in very short duration i.e. 99.9% in 6 minutes which is the acceptance limits for mouth dissolving tablet.

Table 2: Preformulation studies of mouth dissolving tablets of amlodipine & rosuvastatin

Formulation	Bulk density (g/cc) (Avg.±SD)	Tapped density (g/cc) (Avg.±SD)	Carr's index (Avg.±SD)	Hausner's Index (Avg.±SD)	Angle of Repose (Avg.±SD)
F1	0.45±0.01	0.56±0.02	19.64±0.11	1.251±0.01	26.61±0.21
F2	0.50±0.02	0.60±0.03	18.03±0.13	1.200±0.01	29.81±0.16
F3	0.41±0.05	0.51±0.01	19.60±0.16	1.238±0.01	32.90±0.19
F4	0.53±0.01	0.64±0.03	17.18±0.12	1.187±0.01	28.21±0.23
F5	0.45±0.03	0.50±0.01	10.01±0.12	1.101±0.01	35.54±0.16
F6	0.48±0.04	0.56±0.05	14.28±0.11	1.187±0.01	31.61±0.21
F7	0.61±0.01	0.65±0.03	7.69±0.12	1.067±0.01	28.21±0.23
F8	0.54±0.03	0.60±0.01	10.66±0.12	1.105±0.01	29.54±0.16
F9	0.41±0.01	0.52±0.02	20.15±0.11	1.251±0.01	32.61±0.21
F10	0.59±0.03	0.66±0.01	10.62±0.12	1.110±0.01	36.54±0.16
F11	0.47±0.01	0.56±0.05	16.07±0.12	1.187±0.01	31.61±0.21
F12	0.52±0.02	0.61±0.05	14.75±0.01	1.151±0.01	29.90±0.19

Table 3: Post compression studies of mouth dissolving tablets of amlodipine and rosuvastatin

Formulation	Wt variation (mg)(Avg.±SD)	Hardness (kg/cm2) (Avg.±SD)	Friability (%) (Avg.±SD)	Thickness (mm) (Avg.±SD)	Drug content (%) (Avg.±SD)At 237 nm
F1	149.35±0.01	2.5±0.2	0.13±0.11	3.26±0.01	98.3±0.21
F2	155.45±0.02	2.5±0.3	0.09±0.13	3.34±0.06	98.8±0.19
F3	152.92±0.05	2.4±0.2	0.16±0.16	3.26±0.04	96.9±0.16
F4	148.95±0.01	2.5±0.1	0.27±0.12	3.25±0.06	99.5±0.16
F5	148.63±0.03	2.4±0.2	0.28±0.12	3.21±0.01	97.6±0.23
F6	150.46±0.04	2.5±0.2	0.04±0.11	3.18±0.03	98.3±0.21
F7	152.69±0.01	2.5±0.2	0.21±0.12	3.23±0.01	97.6±0.23
F8	149.62±0.03	2.6±0.2	0.40±0.12	3.19±0.05	99.5±0.16
F9	147.37±0.01	2.4±0.2	0.18±0.11	3.30±0.01	96.8±0.16
F10	153.38±0.03	2.5±0.4	0.11±0.12	3.22±0.06	98.4±0.16
F11	151.62±0.01	2.4±0.2	0.07±0.12	3.25±0.03	97.6±0.21
F12	149.02±0.02	2.5±0.2	0.13±0.01	3.21±0.04	99.02±0.21

Table: 4 Post compression studies of mouth dissolving tablets of amlodipine and rosuvastatin

Formulation	Wetting time (sec)(Avg.±SD)	Water absorption ratio (Avg.±SD)	Moisture uptake study (Avg.±SD)	Disintegration time (min. sec) (Avg.±SD)	Drug content (%) (Avg.±SD)AT 244 nm
F1	36.30±0.01	34.14±0.02	3.62±0.11	2.04±0.01	97.6±0.21
F2	32.43±0.02	38.55±0.03	4.14±0.13	1.52±0.01	98.4±0.16
F3	29.15±0.05	37.39±0.01	4.28±0.16	2.09±0.01	101.3±0.19
F4	28.59±0.01	36.71±0.03	5.06±0.12	1.55±0.01	97.6±0.23
F5	36.89±0.03	42.76±0.01	3.62±0.12	1.09±0.01	96.8±0.16
F6	38.63±0.04	44.19±0.05	5.14±0.11	2.63±0.01	98.3±0.21
F7	30.57±0.01	38.32±0.03	4.72±0.12	1.56±0.01	96.3±0.23
F8	31.72±0.03	36.86±0.01	3.51±0.12	1.15±0.01	99.5±0.16
F9	28.98±0.01	35.41±0.02	2.94±0.11	1.35±0.01	97.2±0.21
F10	31.91±0.03	38.82±0.01	4.15±0.12	0.52±0.01	96.9±0.16
F11	29.35±0.01	34.48±0.05	3.07±0.12	0.58±0.01	101.2±0.21
F12	26.98±0.02	36.21±0.05	3.28±0.01	0.47±0.01	98.8±0.19

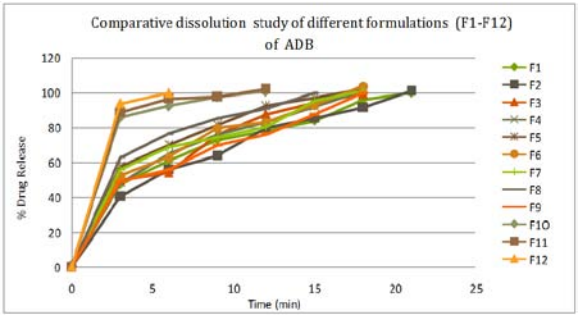

Fig. 2: Comparative *In vitro* dissolution study of mouth dissolving tablets for amlodipine besylate at 237 nm

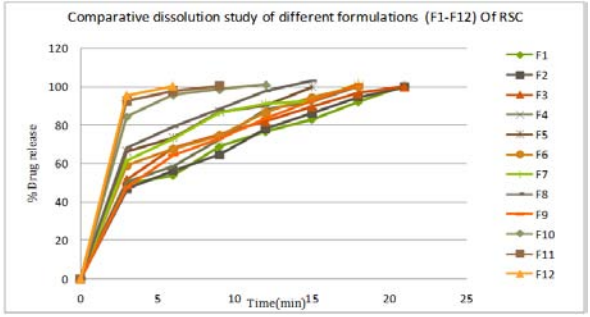

Fig. 3: Comparative *In vitro* dissolution study of Mouth dissolving tablets for Rosuvastatin Calcium at 244 nm

CONCLUSION

Mouth Dissolving tablet of Amlodipine Besylate and Rosuvastatin Calcium were preparedby direct compression method using Croscarmellose Sodium (CCS), Cross povidone(CP), Sodium Starch Glycolate (SSG). The tablet formulation F12 with Sodium Starch Glycolate 5% & Cross Povidone 5% showed greater rate of dissolution at 6 minutes which gives 99.9% drug release. Results from stability studies indicate that the formulated mouth dissolving tablets are stable for a period of 3 months under 2 different conditions at 25±2 °c, 65±5%RH and 40±2 °c and 75±5%RH. There were no remarkable changes were observed during the period of storage. There is no change in physical appearance and % drug release for the period of 3 months, so it is continue for the next three month as per ICH guidelines for stability studies. Cross povidone swell 4-10 folds in less than 10 seconds and it has excellent swelling properties and its high wicking property than Sodium Starch Glycolate at that concentration and Sodium Starch Glycolate show better disintegration time and Swelling of time thus increase the rate of dissolution of formulation.

CONFLICT OF INTERESTS

Declared None

REFERENCES

1. P Ashish, MS Harsoliya, JK Pathan, S Shruti. A review-formulation of mouth dissolving tablet. Int J Pharm Clin Sci 2011;1:1-8.
2. Ajoy Bera, Ashish Mukherjee. A detailed study of mouth dissolving drug delivery system. Acta Chim Pharm Indica 2013;3:65-93.
3. Arijit Gandhi. Mouth dissolving tablets: a new venture in modern formulation technology. Pharma Innovation 2012;1:14-31.
4. Sharma Deepak, Kumar Dinesh, Singh Mankaran, Singh Gurmeet, Rathore. Fast disintegrating tablets: a new era in novel drug delivery system and new market opportunities. J Drug Delivery Ther 2012;2:74-86.
5. Saxene vaubhav, Khinchi Mahaveer, Gupta MK, Agarwal Dilip, Sharma Natasha. “Orally disintegration tablet: friendly dosage form” Int J Res Ayurveda Pharm 2010;1:399-407.
6. Mukesh P Ratnaparkhi, GP Mohanta, Lokesh Upadhyay. “Review on: rapid dissolving tablet”. J Pharm Res 2009;2:63-9.
7. Dali Shukla, Subhashis Chakraborty, Sanjay Singh, Brahmeshwar Mishra. Mouth dissolving tablets i: an overview of evaluation techniques. Sci Pharm 2009;77:327–41.
8. Harlalka SS, Chaware VJ, Deshmane SV, Biyani KR. Formulation and evaluation of orodispersible tablet containing amlodipine besylate. Int J Curr Pharm Res 2014;6:38-41.
9. Ehsan Ali Mohamed. Shaimaa N, Abd Al Hammid. Formulation and evaluation of rosuvastatin orodispersible tablets. Int J Pharm Pharm Sci 2013;5 Suppl 2:339-46.
10. Ganji Amarnath Reddy, Balaji, Naveen Kj, Rajesh Bsb, Yedla Anil Chowdary. Formulation and evaluation of oral fast disintegrating tablets by using amlodipine besylate solid dispersion by direct compression method. Scholars Res Library 2012;4:683-94.
11. Nehal Siddiqui, Garima Garg, Pramod Kumar Sharma. Fast dissolving tablets: preparation, characterization and evaluation: an overview. Int J Pharm Sci Rev Res 2010;4:87.
12. Deshmukh Keshav Ram, Patel Vidyanand. A review on mouth dissolving tabletstechniques. Int J Res Ayurveda Pharm 2013;3;23-32.