Available online at www.elixirpublishers.com (Elixir International Journal)

Pharmacy

Elixir Pharmacy 76 (2014) 28204-28208

ISSN: 2229-712X

Formulation and evaluation of fast dissolving tablets of metoprolol tartrate by direct compression technique

Preethi Jonnakuti[1,*], Debjit Bhowmik[1], S.Duraivel[1], Dipti Ranjan Parida[2] and K.P.Sampath Kumar[3]

[1]Nimra College of Pharmacy, Nimra Nagar, Vijayawada, Andhra Pradesh.

[2]Micro Advance Research Centre, Bangalore.

[3]Department of Pharmacy, Coimbatore Medical College, Coimbatore.

ARTICLE INFO

Article history:

Received: 28 April 2014;

Received in revised form:

25 October 2014;

Accepted: 31 October 2014;

Keywords

Fast dissolving tablets,

Superdisintegrants,

Direct compression technique.

ABSTRACT

The present investigation was undertaken with a view to develop a fast dissolving tablet of Metoprolol Tartrate which offers a new range of product having desired characteristics and intended benefits prepared by direct compression method using different concentrations of superdisintegrant. In the present work Fast dissolving tablets of metoprolol tartrate were prepared by direct compression super disintegrants such as sodium starch glycolate, croscarmellose sodium and crospovidone. All the tablets of metoprolol tartrate were subjected to weight variation, hardness, friability, *in vitro* dispersion, drug polymer interaction, drug content uniformity, and *in vitro* drug release The drug release from tablets of metoprolol tartrate prepared by direct compression was found to be 97.20% of D1 drug release within 10 minute. It is concluded that Metoprolol Tartrate fast dissolving tablets could be prepared using superdisintegrant with improved bioavailability and rapid onset of action.

Introduction

Tablet is the most popular among all dosage forms existing today because of its convenience of self administration, compactness and easy manufacturing; however hand tremors, dysphasia in case of geriatric patients, the underdeveloped muscular and nervous systems in young individuals and h case of uncooperative patients, the problem of swallowing is common phenomenon which leads to poor patient compliance. To overcome these drawbacks, mouth dissolving tablets (MDT) or orally disintegrating tablets (ODT) has emerged as alternative oral dosage forms. These are novel types of tablets that disintegrate/dissolve/ disperse in saliva within few seconds'. According to European Pharmacopoeia, the ODT should disperse/disintegrate in less than three minutes. Therefore, in the present study an attempt will be made to formulate mouth-dissolving tablets of metoprolol tartrate. A antianginal with a view to provide a convenient means of administrations to those patients suffering from difficulties in swallowing such as pediatric, geriatric, uncooperative and patients suffering from angina pectoris. Metoprolol tartrate is effective β-blocker which is having antianginal properties and used in the treatment of myocardial infarction. Oral bioavailability of metoprolol tartrate is around 40%. In present work an attempt has been made to prepare fast dissolving tablets of metoprolol tartrate to enhance the dissolution rate. Tablet disintegrates and disperses in oral cavity within 30 seconds without the need of drinking water. Has pleasant mouth feel and there is no after taste or grittiness.

Materials And Methods

Metoprolol Tartrate procured from Zydus cadila, Ahmedabad, Croscarmellose sodium, Crospovidone gifted sample from Signet chemicals Pvt.ltd,Mumbai, Sodium starch glycolate, Microcrystalline cellulose gifted sample from Maple biotech Pvt.Pune.

Tele:

E-mail addresses: debjit_cr@yahoo.com

Methods of Preparation of Metoprolol Tartarate Fast Dissolvingtablets[2-7]

A) Dry granulation Method:

1. Sifting

Sift Metoprolol Tartarate, Micro crystalline cellulose, crosspovidone, sodium saccharin and talc through mesh #40 separately.

2. Pre-Lubrication

Loaded the sifted materials of step no.1 into suitable into polythene bag and blend for 10 minutes.

3. Sifting

Sift Magnesium stearate through mesh #40 separately.

4. Lubrication

Loaded the sifted Magnesium Stearate of step no. 2 and 3 into polythene bag and mixed for 5 minutes.

5. Compression

The lubricated blend of step no.4 was compressed using following parameters:

Evaluation of Tablets:[5-12]

To design tablets and later monitor tablet production quality, quantitative evaluation and assessment of tablet chemical, physical and bioavailability properties must be made.The important parameters in the evaluation of tablets can be divided into pysical and chemical parameters.

Physical appearance:

The general appearance of tablets, its visual identity and overall elegance is essential for consumer acceptance. The control of general appearance of tablet involves measurement of number of attributes such as tablet size, shape, colour, presence or absence of odour, taste, surface texture and consistency of any identification marks.

Hardness test:

This is the force required to break a tablet in a diametric compression. Hardness of the tablet is determined by Stock's Monsanto hardness tester which consists of a barrel with a compressible spring. The pointer moves along the gauze in the

barrel fracture. The tablet hardness of 7Kp is considered as suitable for handing the tablet.

Tablet size and Thickness:

Control of physical dimensions of the tablets such as size and thickness is essential for consumer acceptance and tablet-tablet uniformity. The diameter size and punch size of tablets depends on the die and punches selected for making the tablets. The thickness of tablet is measured by Vernier Callipers scale. The thickness of the tablet related to the tablet hardness and can be used an initial control parameter. Tablet thickness should be controlled within a ±5%. In addition thickness must be controlled to facilitate packaging.

Friability:

This test is performed to evaluate the ability of tablets to withstand abrasion in packing, handling and transporting. Initial weight of 20 tablets is taken and these are placed in the friabilator, rotating at 25rpm for 4min. The difference in the weight is noted and expressed as percentage. It should be preferably between 0.5 to 1.0%.

%Friability = (W1-W2)/W1 X 100

Where, W1= weight o f tablets before test

W2 = weight of tablets after test

Weight variation of Tablets:

It is desirable that all the tablets of a particular batch should be uniform in weight. If any weight variation is there, that should fall within the prescribed limits:

Twenty tablets were taken randomly and weighed accurately. The average weight was calculated by,

$$\text{Average weight} = \frac{\text{weight of 20 tablets}}{20}$$

Disintegration test:

Disintegration time is considered to be one of the important criteria in selection the best formulation. To achieve correlation between disintegration time in-vitro and in-vivo, several methods were proposed, developed and followed at their convenience. One tablet was placed into each tube and the assembly was suspended into the 1000ml beaker containing water maintained at 37±20^{o}c and operated the apparatus for 15 minutes. The assembly was removed from the liquid and the tablets were observed. If one or two tablets fail to disintegrate completely, repeat the test on 12 additional tablets. The requirement is met if not less than 16 of the total of 18 tablets tested are disintegrated.

Wetting time:

A piece of tissue paper folded twice was kept in a petridish containing 6 ml 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.

In-dispersion time:

The in vitro dispersion time was measured by dropping tablet in a beaker containing 100ml of water and stirring gently. The time for the tablet to completely disperse into fine particles was noted.

Results And Discussion

Conclusion: Based on compressibility index and particle size distribution data, it was concluded that the blend showed good flow characteristics. Thus, the blend was compressed further to check the compression parameter.

B) Sublimation method

Blend Uniformity:

Blend Uniformity during pre-lubrication: Uniformity of the blend during the prelubrication stage was analysed and the results were presented in the following table:

Minimum: 95.4% w/w

Maximum: 100.2 % w/w

Blend Uniformity during lubrication: Uniformity of the blend during the lubrication stage was analysed and the results were presented in the following table:

Minimum: 96.9% w/w

Maximum: 100.1% w/w

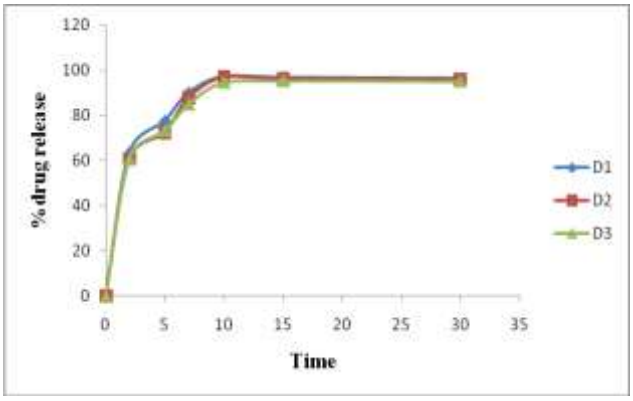

Fig 1: In vitro dissolution studies of the formulations prepared by direct compression method using Crosspovidone

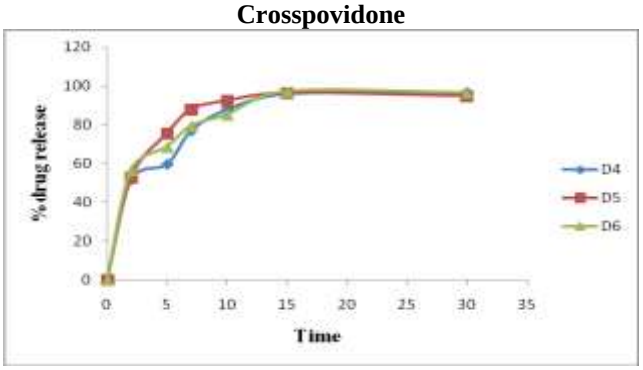

Fig 2. In vitro dissolution studies of the formulations prepared by direct compression method using Crosscarmellose sodium

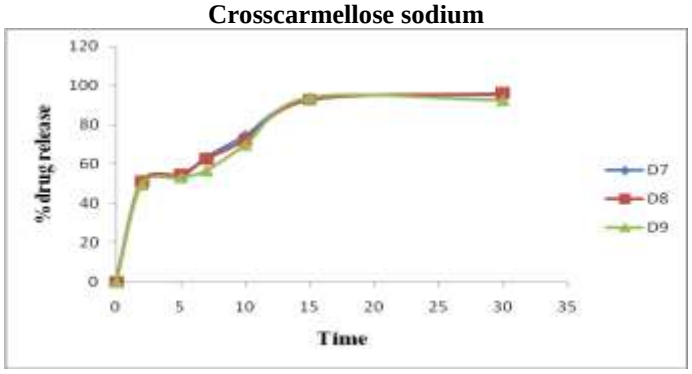

Fig 3: In vitro dissolution studies of the formulations prepared by direct compression method using Sodium starch glycolate

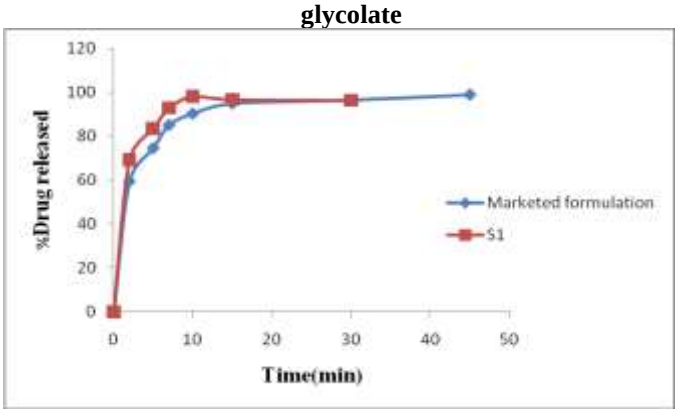

Fig 4. In vitro dissolution comparison studies of the optimized formulation and marketed

Conclusion

In the present work Fast dissolving tablets of Metoprolol tartrate were prepared by direct compression using super disintegrants such as sodium starch glycolate, croscarmellose sodium and crospovidone. The drug release from tablets of metoprolol tartrate prepared by direct compression and sublimation methods were found to be 97.20% of D1 drug release within 10 minute.

Table 1. Compression parameters

Tooling	8 mm round shaped standard concave punches
Weight of individual tablet	200 mg ± 5%
Thickness	4.0±0.3 mm
Hardness	6-8 kp
Friability	Not more than 1%
DT	Not more than 15 min

Table 2. Composition of Formulations for Direct Compression

S. No	Ingredients	D1	D2	D3	D4	D5	D6	D7	D8	D9
1.	Metoprolol tartarate	25	25	25	25	25	25	25	25	25
2.	Microcrystalline cellulose USP- NF(Avicel PH 102)	154	149	144	154	149	144	154	149	144
3.	Crosspovidone	5	10	15	-	-	-	-	-	-
4.	Croscarmellose sodium USP- NF	-	-	-	5	10	15	-	-	-
5.	Sodiumstarch gycoate	-	-	-	-	-	-	5	10	15
6.	Sodium Saccharin	10	10	10	10	10	10	10	10	10
7.	Talc	2	2	2	2	2	2	2	2	2
8.	Magnesium stearate USP-NF	4	4	4	4	4	4	4	4	4
	Tablet weight	200	200	200	200	200	200	200	200	200

Table 8: Acceptance criteria for tablet weight variation

Average weight of tablet(mg)	Maximum % difference allowed
130 or Less than	± 10
130-324	± 7.5
More than 324	± 5

Table 3. Pre compression parameters of the formulations prepared by Direct compression

Formulation	Angle of repose	Bulk density	Tapped density	Compressbility index	Hausners ratio
D1	33.2±0.04	0.37±0.04	0.45±0.04	18.7±0.02	1.2±0.02
D2	34.3±0.04	0.35±0.08	0.46±0.02	19±0.02	1.12±0.08
D3	32.0±0.04	0.39±0.04	0.48±0.02	17.7±0.08	1.21±0.02
D4	32.6±0.02	0.36±0.12	0.47±0.02	18.6±0.02	1.19±0.12
D5	31.9±0.08	0.35±0.02	0.49±0.02	17.6±0.12	1.32±0.02
D6	33.8±0.12	0.38±0.04	0.43±0.02	19.6±0.02	1.24±0.08
D7	32.5±0.12	0.33±0.12	0.47±0.08	18.8±0.08	1.34±0.02
D8	30.2±0.12	0.34±0.02	0.45±0.08	17.7±0.02	1.24±0.12
D9	29.9±0.08	0.38±0.02	0.49±0.08	19±0.02	1.09±0.02

Table 4. Particle size distribution

Sieve No.	Cumulative retentions
20	18.21%
30	39.21%
40	54.33%
60	66.64%
80	71.13%
100	72.91%
Receiver	100%

Table 5. Data showing the result of blend uniformity during Pre-lubrication

S.No	Trials	Assay%(w/w) Of Metoprolol tartarate
Time (min) ⟶		Prelubrication time 10 Min
1.	S1	97.0
2.	S2	95.4
3.	S3	98.4
4.	S4	97.0
5.	S5	97.0
6.	S6	95.4
7.	S7	98.4
8.	S8	100.2
9	S9	99.3

Minimum: 95.4% w/w
Maximum: 100.2 % w/w

Table 6. Data showing the result of blend uniformity during lubrication

S.No	Trials	Assay% (w/w) of Metoprolol tartarate
Time (min) ⟶		Lubrication time 5 Min
1.	S1	97.8
2.	S2	100.1
3.	S3	97.8
4.	S4	98.6
5.	S5	96.9
6.	S6	97.8
7.	S7	97.8
8.	S8	97.6
9.	S9	99.9

Minimum: 96.9% w/w
Maximum: 100.1% w/w

Table 7. Post-Compression Parameters of Tablets Prepared By Direct Compression

Formulation	Average Hardness (Kp)	Thickness (mm)	Percentage of weight loss (%)	Average Weight (mg)	In-vitro dispersion time(sec)	Disintegration time(sec)	Wetting time(sec)	Assay (%)
D1	3.8±0.09	4.2-4.4	0.02±1.27	200.1	48	45	20	99.7
D2	3.4 ± 0.05	4.2-4.4	0.05±0.01	200.3	49	40	23	101.3
D3	3.5 ± 0.32	4.1-4.4	0.04±0.11	204.1	38	34	21	99.5
D4	3.5 ± 0.12	4.3-4.4	0.02±0.02	202.3	79	74	35	98.6
D5	3.6 ± 0.08	4.3-4.4	0.01±0.05	201.1	74	69	36	98.5
D6	3.8 ± 0.33	4.3-4.4	0.01±0.06	203.3	59	54	37	101.9
D7	3.9 ± 0.25	4.3-4.4	0.03±0.05	202.1	96	90	42	98.6
D8	3.7 ± 0.12	4.3-4.4	0.04±0.012	204.3	99	96	42	100.5
D9	4.0 ±0.33	4.3-4.4	0.01±0.06	205.1	117	112	41	101.5

References

Rao TV, Vidhyadhara S. Formulation and evaluation of mouth dispersible tablets of simvastatin by direct compression technique. The Pharma Review. 2008: 137-9.

Patel DM, Patel NM, Shah RR, Jogani PD and Balapatel A. Studies in formulation of Orodispersible tablets of rofecoxib. Indian J Pharm Sci. 2004; 66(5): 621-5.

Rampure MV, Raju SA, Shirsand SB, Swamy PV and Nagendrakumar. Rapidly disintegrating oral tablets of alfuzosin. The Pharma Review. 2008: 140-2.

Raghavendra Rao NG, Patel T, Gandhi S. Development and evaluation of carbamazepine fast dissolving tablets prepared with complexes by direct compression technique. Asian J Pharm. 2009; 3(3): 97-103.

Deshmukh SS, Potnis VV, Mahaparale PR, Kasture PV and Gharge VS. Development and evaluation of ziprasidone hydrochloride fast disintegrating/ dissolving tablets using complexation techniques. Indian J Pharm Educ Res. 2009; 43(3): 300-7.

Vamshi Priya VA, Chandrasekhara Rao G, Srinivas Reddy D, Prabhakar Reddy V. The effect of superdisintegrants and their concentration on the dissolution of topiramate immediate release tablets. Int J Pharm Sci & Nanotechnology. 2003; 2(2): 531-36.

Balasubramanium J, Bindu K, Rao VU, Ray D, Halder R, Brzeczko AW. Effect of superdisintegrants on dissolution of cationic drugs. Dissolution Technologies 2008; 15(2): 18-25.

Sweetman SC (eds.). Martindale – The Complete Drug Reference. 33 rd edn.; 2002: 931-2.

Vijaya KS, Mishra DN. Rapidly disintegrating oral tablets of meloxicam. Indian Drugs. 2006; 43(2): 117-21.

Lachman L, Libermann HA, Kanig JL. The theory and practice of industrial pharmacy. Varghese Publishing House, 3 rd edition; 1991; 297-301.

Sarasija S, Pandit V, Joshi HP. Preparation and evaluation mouth dissolving tablets of salbutamol sulphate. Indian J Pharm Sci. 2007; 69(3): 467-9.

Yunxia B, Hisakazu S, Yorinobu Y, Kazumi D, Akinobu O, Kotaro I. Preparation and evaluation of compressed tablet rapidly disintegrating in the oral cavity. Chem Pharm Bull 1996; 44(11): 2121-7