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Pharmacy

Elixir Pharmacy 70 (2014) 24043-24046

ISSN: 2229-712X

Formulation and evaluation of mouth dissolving tablets of metoprolol tartrate by sublimation technique

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ARTICLE INFO

Article history:

Received: 23 November 2013;

Received in revised form:

25 April 2014;

Accepted: 5 May 2014;

Keywords

Fast dissolving tablets,

Sublimation technique,

Metoprolol Tartrate.

ABSTRACT

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. Sublimation method . The values of pre-compression parameters evaluated were within prescribed limits and indicated good free flowing property. In all the formulations, friability is less than 1%, indicated that tablets had a good mechanical resistance. Drug content was found to be in the range of 98 to 102%, which is within acceptable limits. In sublimation method, camphor is used as subliming agent. 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 sublimation methods were found to be S1 showed 98.20% drug release within 10 minute. It is concluded that Metoprolol Tartrate mouth dissolving tablets could be prepared using sublimation technique with improved bioavailability and rapid onset of action.

Introduction

Metoprolol tartrate(MT) is a selective beta1-adrenoreceptor blocking agent. Metoprolol tartrateis used in Essential hypertension, prevention after a myocardial infarction, tachycardia, coronary heart disease (prevention of angina attacks), treatment of heart failure. The metoprolol tartratefreely soluble in water and extensively absorbed after oral administration. The absolute oral bioavailability is only approximately 40% due to extensive hepatic metabolism. having half life 3 to 5 hrs. In present work Fast dissolving tablets of metoprolol tartrateare formulated by Direct compression and sublimation methods that disperse rapidly when placed below tongue. The basis of sublimation technique is to add inert solid ingredients that volatilize readily (eg camphor, ammonium bicarbonate, naphthalene, urea, urethane etc) to other tablet excipients and the mixture is then compressed into tablets. Volatile material is then removed via sublimation which generates a porous structure applied the sublimation technique to prepare highly porous compressed tablets that were soluble in saliva. MCC and camphor were used as a tablet matrix material and subliming the material respectively.

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.

Methods of Preparation Of Metoprolol Tartarate Fast Dissolving tablets Sublimation Method:

1. Sifting Sift Metoprolol Tartarate, Micro crystalline cellulose, Crosspovidone, Sodium saccharin,Camphor 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. The compressed tablets were than subjected to sublimation at 80° c for 30 min.

Evaluation of Tablets:

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.

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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°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.

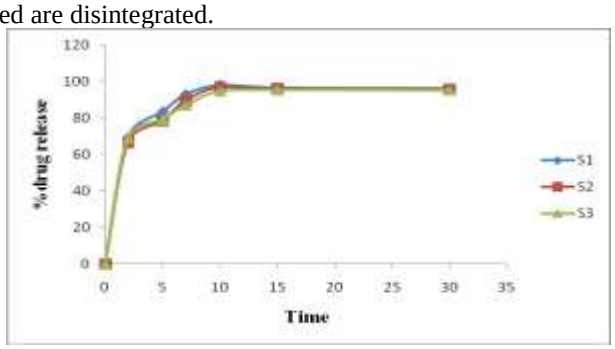

Fig14: In vitro dissolution studies of the formulations prepared by Sublimation method using Crosspovidone

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:

bsed 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.

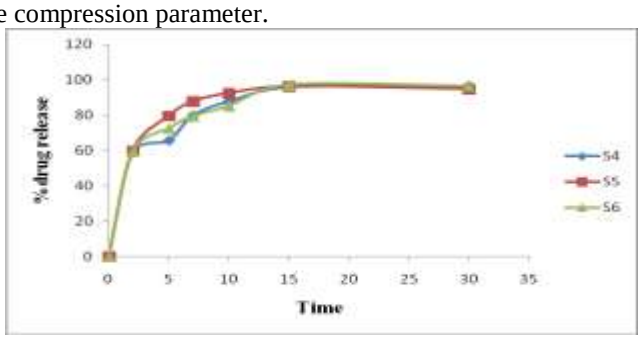

FIG 15:In vitro dissolution studies of the formulations prepared by Sublimation method using Crosscarmellose sodium.

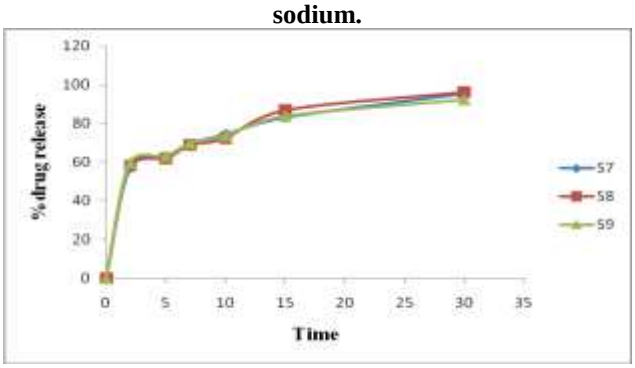

FIG16:In vitro dissolution studies of the formulations prepared by Sublimation method using Sodium starch glycolate

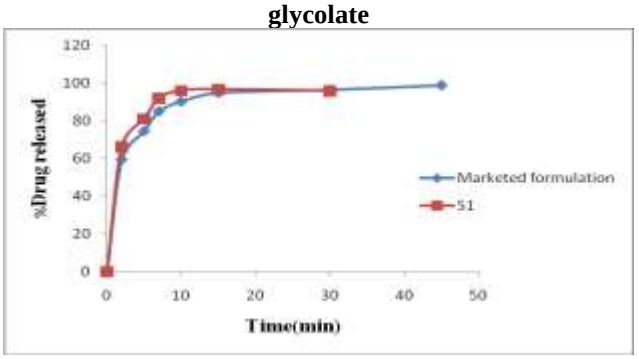

FIG18:In vitro dissolution comparison studies of the optimized formulation after stability study (S1) and marketed

Conclusion

In the present work Fast dissolving tablets of metoprolol tartrate were prepared by direct compression and sublimation methods .In sublimation method, camphor is used as subliming agent. The drug release from tablets of metoprolol tartrate prepared by sublimation methods were found to be 98.20% 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 Sublimation Method

S. No	Ingredients	S1	S2	S3	S4	S5	S6	S7	S8	S9
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.	Camphor	20	20	20	20	20	20	20	20	20
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 3. 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 23: Pre compression parameters of the formulations prepared by Sublimation compression:

Formulation	Angle of repose	Bulk density	Tapped density	Compressbility index	Hausners ratio
S1	31.9±0.08	0.35±0.02	0.49±0.08	17.6±0.12	1.32±0.02
S2	33.8±0.12	0.38±0.04	0.47±0.02	19.6±0.02	1.24±0.08
S3	32.5±0.12	0.33±0.12	0.44±0.08	18.8±0.08	1.34±0.02
S4	30.2±0.12	0.34±0.02	0.43±0.08	17.7±0.02	1.24±0.12
S5	29.9±0.08	0.38±0.02	0.49±0.08	19.0±0.02	1.09±0.02
S6	31.9±0.08	0.35±0.02	0.47±0.02	17.6±0.12	1.32±0.02
S7	31.5±0.12	0.36±0.12	0.47±0.02	19.6±0.02	1.34±0.02
S8	32.2±0.12	0.38±0.02	0.44±0.08	17.7±0.02	1.24±0.12
S9	29.7±0.08	0.36±0.02	0.43±0.08	19.0±0.02	1.09±0.02

Particle size distribution

Sieve No.	Cumulative retentions
20	**16.21%**
30	**40.21%**
40	**55.33%**
60	**64.64%**
80	**73.13%**
100	**75.91%**
Receiver	**100%**

Table 25:Post-Compression Parametrs of Tablets Prepared by Sublimation Method

Formulation	Average Hardness (Kp)	Thickness (mm)	Percentage of weight loss (%)	Average Weight (mg)	Wetting time (sec)	In-vitro dispersion time(sec)	Disintegration time(sec)	Assay (%)
S1	3.2±0.09	4.0-4.2	0.01±1.27	199.1	30	43	38	98.7
S2	3.0 ± 0.05	4.1-4.4	0.04±0.01	198.3	25	39	32	100.3
S3	3.2 ± 0.32	4.0-4.3	0.06±0.11	204.1	24	31	28	98.5
S4	3.5 ± 0.12	4.1-4.4	0.01±0.02	200.3	60	72	68	99.6
S5	3.4 ± 0.08	4.2-4.4	0.08±0.05	201.1	57	69	64	99.5
S6	3.3 ± 0.33	4.0-4.3	0.02±0.06	202.3	42	48	45	100.9
S7	3.1 ± 0.25	4.3-4.4	0.03±0.05	200.1	78	89	85	99.6
S8	3.4 ± 0.12	4.3-4.4	0.08±0.012	201.3	85	96	90	101.5
S9	3.2 ±0.33	4.2-4.4	0.01±0.06	202.1	100	110	105	100.5

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