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Research Article

Formulation Development and In-Vitro Evaluation of Metoprolol Succinate Sustained Release Tablets

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Abstract

Metoprolol succinate is a cardio selective β-blocker used in the management of secondary hypertension complications. Metoprolol succinate is prescribed to suppress the hypertension condition and to minimize the cardiac related disorder. In the present study, metoprolol succinate sustained-release tablets were successfully prepared by the wet granulation method. HPMC and ethyl cellulose were used as drug release modifying polymers in varying ratios. All developed tablets were passed the uniformity of weight, friability, uniformity of thickness, and uniformity of diameter test respectively. The crushing strength of formulated tablet was in ranges of 1.2 to 2.6 and showed the optimum tensile strength. The formulated tablet's percentage of drug content and content of uniformity had 98.50 and 99.12.The formulated batch F2 capable for provide the desirable drug release up to 20 hours period. The stability study shows the formulation batch F2 was stable. Therefore, this formulation method is economically it may be suitable for the pharmaceutical industries to use this type of simple technology for the development of advanced formulations

Keywords: Metoprolol succinate, HPMC, Ethyl cellulose, Sustained release tablet, Matrix tablet

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1. Introduction

Sustained drug delivery system that achieves slow release of drug over an extended period of time with emergence to effectively cured disorder condition and ensure that comply patient compliances with their medication [1]. The system is capable to deliver a steady plasma concentration and avoid differential fluxes in plasma concentration of conventional dosage form. These systems are fruitful to patients for increasing their compliances to medication. Daily once dose of sustained drug delivery system makes sure that patients do not avoid their medication. Additionally, formulate matrix tablet of sustained release dosage forms has unique innovation for novel drug delivery systems [2]. Matrix formulation is composition of

one or more drugs with using gelling agent such as hydrophilic polymers [3]. In matrix tablet, excluding multifaceted production procedures such as coating and palletization throughout manufacturing. In the formulation used different type and ratio of polymer which is controlled the drug release rate from the dosage form [4]. The role of hydrophilic polymers in sustained release matrix tablet was to discharge the drugs in a steady and consistent way for to achieve constant peak plasma level.

2. Materials and methods

Metoprolol succinate was obtained from Zim Laboratories, Nagpur. HPMC K30 & HPMC K100 were obtained from Hetero labs from Hyderabad, Ethyl cellulose, microcrystalline cellulose, Talc powder and Magnesium stearate were obtained from LobaChem, Mumbai. All other reagents and chemicals were of analytical grade. Double distilled water was used throughout the study.

Methods:

Formulation and evaluation of tablet granules:

The formulation of metoprolol succinate sustained release matrix tablets were successfully done by wet granulation method [8]. All of the above ingredients (Table 1) were weighed and mixed in dilution according to the method. Using granulating fluid (water) mixed thoroughly to prepare a wet mass. Afterwards, the wetted granules were dried up for 1h at 60°C. Metoprolol succinate prepared granules for tablets were evaluated using numerous methods. Further, evaluation of prepared granules carried out by determination of angle of repose according to fixed height method. The bulk and tapped densities were used for the determination of percentage of compressibility [9]. Single punch tableting machine was used to compress the granules into tablets. Lubricants and glidants were added before to compression process.

Metoprolol sustained release matrix tablets were prepared using 150 mg of metoprolol succinate and concentration of polymer and excipients as shown in Table .Drug release modifying polymers HPMC & ethyl cellulose in varying ratio was used for different formulation. Microcrystalline cellulose was used as diluent whiles magnesium stearate and talc were used a lubricant and glidant respectively.

Pre-formulation Study:

Bulk Density: Bulk density is the ratio of the mass by the volume of an untapped powder sample. The bulk density is measured in g/ml. The bulk density depends on both the density of the powder particles and the arrangement of the powder particles. The bulk density influences preparation, storage of the sample. The mathematical re-presentation is given below.

Bulk density = weight of the drug / Bulk volume

Tapped Density:

In tapped density, the bulk powder is mechanically tapped in a graduated cylinder until the volume change is observed. Here the tapped density is calculated as mass divided by the final volume of the powder.

Tapped density = weight of the granules / tapped volume

Angle of Repose:

It gives an idea of the flowability of granules or a bulk solid. There is some factor which responsible for the flowability of powders such as particle size, shape, surface area, etc. The flowability of the powder depends on the different environments and can be changed easily. The angle of repose was calculated by the following formula.

$\theta = \tan^{-1} h/r$

Where = θ = angle of repose, h = height of the formed cone, r = radius of the circular base

Carr's Index:

It is one of the most important parameters to characterize the nature of granules.

Carr's index (%) = (Tapped density - Bulk density/ Tapped density) × 100Hausner's ratio

It is an important character to determine the flow property of granules in the presence of different compositions of polymers. The following formula can calculate this.

Hausner's ratio = Tapped density / Bulk density

Values less than 1.25 indicate good flow, and greater than 1.25 indicate poor flow.

Post-compression Study:

Weight Variation Test: Twenty tablets were selected randomly from each formulation and weighed individually using a digital balance (Shimadzu AUY 220, Uni Bloc, Germany). The average weights were calculated, and mean values were determined. It should not deviate more than ± 5% as per the Indian Pharmacopeia (IP).

Tablet Thickness Test: To determine the uniformity and physical dimension of tablet, thickness is measured by Vernier calipers for randomly selected 20 tablets from each formulation.

Hardness Test:

Hardness is determined to measure the strength of a tablet for randomly selected 10 tablets from each formulation using Monsanto Hardness Tester 24.

Tablet Friability:

Previously weighed 10 tablets were placed in Roche's friabilator for 15 min/ 100 rpm. The tablets were de-dusted and accurately weighed. The % loss was calculated as per IP. It is expected to be less than 1%.

Drug Content Uniformity:

Ten tablets from each formulation were crushed and dissolved in water. The solution was filtered, and the drug content was determined by UV spectrophotometer (Jasco V-670, Japan) at 232 nm with a suitable dilution.

***In-vitro* Dissolution Test:**

Drug release studies for all formulations were determined using USP type II dissolution. Secor India Lab) at 100rpm bearing 900 ml of pH 2 or pH 6.8 medium at 37 ± 0.5 °C. At regular intervals of time, 5 ml samples were withdrawn and replaced by fresh solution, and the absorbance was measured at 232 nm.

3. Results and Discussion

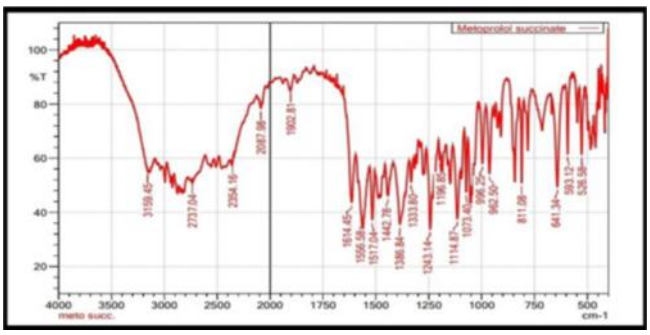

Figure 1

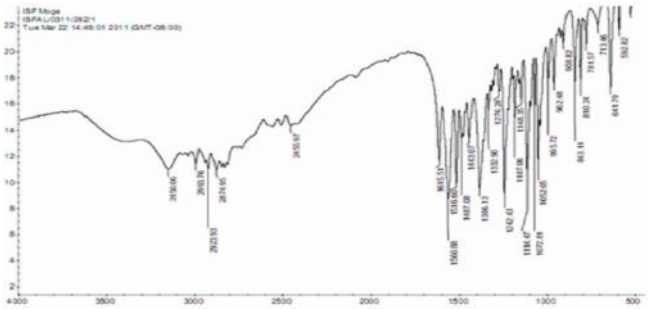

Figure 2

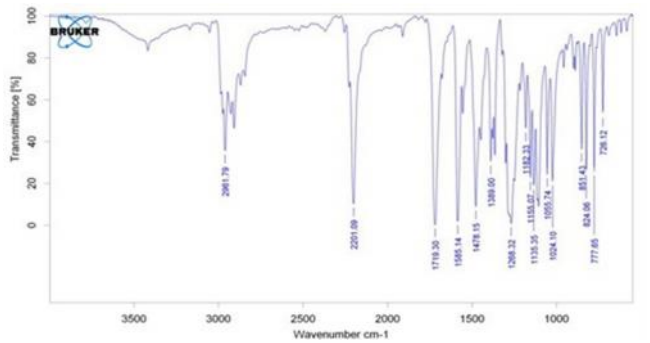

Figure 3

The formulated granules were evaluated physically to their flow properties which suitable for the tablets for compression [19]. The compressibility index, angle of repose and the Hausner's ratio indicated that F1, F2, F3 and F7 granules had a good flow, F4, F5 and F6 granules had a excellent flow properties show in Table.

***In vitro* dissolution studies:**

HPMC K30, HPMC K100 and ethyl cellulose different ratio was taken to formulate the metoprolol succinate sustained release matrix tablets (F1-F7). In dissolution study, multiple parameters were used to measure the dissolution specification for controlled release drug. Entire formulated batches were capable to deliver a sustained release over 20 hour period. Although, batches F1 to F3 were qualify to particular time point's measures of putative pharmacopoeia limits also the result was compared with the standard drug (Antiblok). These measures indicated that their drug release should be in between 10-30 % within primitive two hours, at eight hours should be 50% drug release and near to 80% after twelve hours. Formulated batches F4 to F5, drug release was unable to reach.

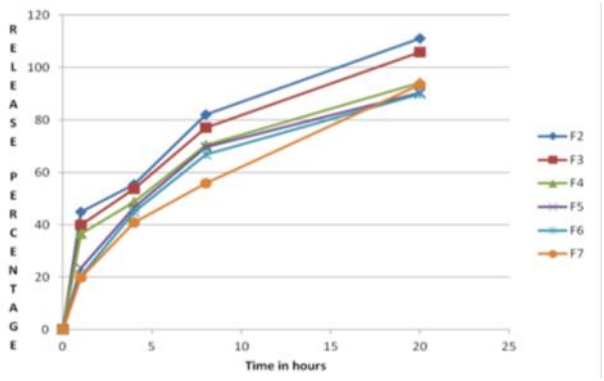

Figure 4: In Vitro drug release studies

Table 1: Formulation of Metoprololsuccinat sustained release tablets

S.NO	ingredient	1	F2	F3	F4	F5	F6	F7
1	Metoprolol succinate	150	150	150	150	150	150	150
2	HPMC K30	20	30	40	5	5	5	25
3	Ethyl cellulose	30	20	10	40	30	20	20
4	HPMC K100	25	25	25	30	40	50	50
5	Talc	10	10	10	10	10	10	10
6	Magnesium Stearate	15	15	15	15	15	15	15
7	Total weight (mg)	250	250	250	250	250	250	250

Table 2: Evaluation of granules of Metoprololsuccinat

Formulations	Parameters				
	Angle of Repose θ	BD(g/ml)*	TD(g/ml)*	CI (%)*	HR*
F-1	31.96±0.23	0.63±0.02	0.75±0.02	16.78±0.13	1.18 ± 0.01
F-2	25.56±0.21	0.51±0.02	0.61±0.04	15.12±0.04	1.17 ± 0.01

F-3	25.2±0.13	0.55±0.00	0.66±0.01	13.63±0.11	1.12 ± 0.02
F-4	25.24±0.19	0.54±0.01	0.65±0.01	15.66±0.15	1.32± 0.01
F-5	22.1±0.21	0.55±0.01	0.64±0.00	14.06±0.05	1.16±0.02
F-6	25.8±0.23	0.53±0.01	0.61±0.01	12.66±0.13	1.12 ± 0.01
F-7	21.5±0.28	0.52±0.02	0.63±0.04	20.31±0.04	1.25 ± 0.01

Table 3: Physical Properties of formulated Metoprolol succinate SR matrix tablets

Formulation code	Thickness	Diameter	Hardness	Friability	Drug content
F1	2.9±0.02	8.21±0.2	4.23±0.14	0.495±0.044	96.25
F2	3.5±0.01	8.12±0.23	4.17±0.09	0.530±0.046	99.24
F3	3.7±0.03	8.05±0.2	4.36±0.10	0.483±0.058	98.01
F4	3.3±0.02	8.04±0.34	4.44±0.13	0.522±0.029	95.12
F5	3.5±0.01	8.11±0.2	4.67±0.11	0.782±0.031	93.43
F6	3.1±0.02	8.33±0.13	4.67±0.08	0.713±0.023	98.23
F7	3.3±0.02	8.11±0.2	4.45±0.08	0.782±0.031	98.12

Table 4: Evaluation of *In vitro* dissolution of ER tablets of Metoprololsuccinate: F-1toF-9

TESTS	F-1	F-2	F-3	F-4	F-5	F-6	F-7
1st Hr	6	6.2	7	3.2	1.5	4.8	6.9
2nd Hr	7.2	11.1	11	6	5.6	9.3	12.2
4th Hr	14	12.4	21.3	11.4	11.3	21.4	27
6th Hr	35.1	33.2	38	29	27.1	36	38.1
8th Hr	48	55.1	47	57	46.2	49.1	48
12th Hr	67.4	77	64.6	73	72	69	70
16th Hr	82	90	77.1	84.2	81	83	83.6
20th Hr	89.1	100	88	87.3	87	88.2	90

4. Conclusion

Metoprolol succinate sustained release matrix tablets have been successfully formulated using Ethyl cellulose, HPMC K30 and HPMC K100 respectively. Although, the formulated batch F2 which are capable for provide the desirable drug release and stable over a 20 hours period. Another, formulated batches has retarded the drug release and did not provide the desirable drug release after 20 hours period.

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