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Research Article

Formulation and Evaluation of Orally Disintegrating Tablets of Atenolol with Cyclodextrine Inclusion Complex

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Abstract

Orally disintegrating tablets of atenolol with cyclodexdrine inclusion complex were formulated for the management of hypertension. In the formulation of Sodium Starch Gycolate,crospovidone, Croscarmellose sodium were used as super disintegrant.and cyclodextrine used as a inclusion complexing agent. Preformulation studies were performed prior to compression. The compressed Tablets were evaluated for weight variation, hardness, friability, drug content, disintegration time and *in-vitro* drug release using USP dissolution apparatus type 2 (paddle). It was found that the optimized formulation showed 99.88% release for Atenolol at the end of 15 mins. The IR spectrum studies revealed that there is no disturbance in the principal peaks of pure drugs Atenolol. This further confirms the integrity of pure drugs and no incompatibility of them with excipients.

Key Words: Atenolol,β cyclodextrine,SSG, Crospovidone, Croscarmellose sodium

Introduction

The oral route of administration is considered as the most widely accepted route because of its convenience of self administration, compactness and easy manufacturing. But the most evident drawback of the commonly used oral dosage forms like tablets and capsules is difficulty in swallowing, leading to patients incompliance particularly in case of pediatric and geriatric patients, but it also applies to people who are ill in bed and to those active working patients who are busy or traveling, especially those who have no access to water.

A solid dosage form containing medicinal substance or active ingredient which disintegrates rapidly usually within a matter of seconds when placed upon the tongue." The disintegration time for ODTs generally ranges from several seconds to about a minute[1]

Hypertension is the most common cardiovascular disease; its prevalence increases with advancing age. Hypertension is the principal cause of stroke, is a major risk factor for coronary artery disease and its complications, and is a major contributor to cardiac failure, renal insufficiency, and dissecting aortic aneurysm. Hypertension is defined as a sustained increase in blood pressure ≥140/90 mm Hg[2]

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Literature survey shows that, Atenolol, a competitive beta(1)-selective adrenergic antagonist, has the lowest lipid solubility of this drug class

atenolol competes with sympathomimetic neurotransmitters such as catecholamines for binding at beta(1)-adrenergic receptors in the heart and vascular smooth muscle, inhibiting sympathetic stimulation. This results in a reduction in resting heart rate, cardiac output, systolic and diastolic blood pressure, and reflex orthostatic hypotension. Higher doses of atenolol also competitively block beta(2)-adrenergic responses in the bronchial and vascular smooth muscles.

Atenolol short half life i.e. 6 hrs. So, to Reduce frequency of administration of drug in a day fast release tablet of Atenolol is formulated.

The present work aims to develop a stable and optimized orally disintegrating tablet of Atenolol form containing cyclodextrine complexing agent.

Material and Method

Atenolol were received from Ami lifesciennce, Cyclodextrine, SSG, Crospovidon, Cramellose Sodium received from Cyno Pharma Pvt., Indore.

Fourier transforms infrared (FT-IR) spectroscopy

Compatibility studies were carried out to know the possible interactions between Atenolol and excipients used in the formulation. Physical mixtures of drug and excipients were prepared to study the compatibility. Drug polymer compatibility studies were carried out using FT-IR spectroscopy. IR spectrum of pure drug and polymers was seen in between 600- 4000 cm^{-1}.

Preparation of Tablets

Formulation of Drug-Cyclodextine Inclusion Complex:

Atenolol and CD's were sieved through #120 prior to their use. Complaxes of β-CD with Atenolol were prepared in the molar ratio og 1:1 by different methods mentioned below. For better identification, the samples are designated with different abbreviations[3]

Physical mixture: Physical mixture of CD's and Atenolol were prepared by simply mixing powders with a spatula for 15 min and then sieved through 120#.

Formulation of Orally Disintegreting Tablet:

Atenolol orally disintegrating tablets were prepared by direct compression metood. Different concentration of excipients was used to prepare different groups of orally disintegrating tablets., composition of various formulation are shown in Table. All the ingradients of orally disintegrating tablets of Atenolol were weighed and

mixed.Finally Magnesium Sterate and Aerosil are added and compressed using tablet punching machin. The total weight of the formulation was maintaind 200mg.[4]

Weight variation Twenty tablets of each formulation were weighed using an electronic balance and average weight of ten tablets and standard deviation were calculated [5]

Thickness Thickness of each formulation was measured using digital caliper. Ten bilayer tablets from batch were used and average values were calculated.

Hardness The hardness of the tablets was determined using Schleuniger hardness tester. It was expressed in Newton (N).

Friability The friability of tablets was determined using Roche friabilator. It is expressed in percentage (%). About 20 tablets ($W_{initial}$) were transferred into friabilator. The friabilator was operated at 25 rpm for 4 minutes or run up to 100 revolutions. The tablets were dedusted and weighed again (W_{final}).[6]

Disintegration test It is determined by using USP device which consist of 6 glass tubes that are 3 inches long, open at one end and held against 10 mesh screen at the bottom end of basket rack assembly. To test for disintegration time, one tablet is placed in each tube and the basket arch is positioned in a1 liter beaker of water at 37°C ± 2°C.A standard motor driven device is used to move the basket assembly up and down. To be incompliance with the USP standard, all tablets must disintegrate and all particles must pass through the 10 mesh in the time specified[7]

In vitro dissolution study of tablets Release from Atenolol the fast dissolving tablets was studies in 0.1N HCL (900 ML) using USP single station Dissolution Rate Test Apparatus with a rotating paddle stirrer at 50 rpm and 37^0C±0.5^0C. A sample of dissolution fluid were withdrawn through a pipette at different time intervals and were assayed a 225 nm for Atenolol drug content using a UV/Visible spectrophotometer. A sample (5ml) of the solution was withdrawn from the dissolution apparatus at 2, 4, 6, 8 and 10 min and withdrawn was replaced with fresh dissolution media. Absorption of filtered solution was checked by UV spectroscopy.[8,9]

Results and Discussion

The main aim of this work was to prepare orally disintegrating tablets of atenolol with cyclodextrine inclusion complex.

Drug polymer compatibility studies using FTIR

All the characteristic IR peaks related to pure drug, were also appear in the IR spectrum of mixture of Drug-excipients so there was no any chemical incompatibility between drug, polymer and excipients (Fig 1).

Weight variation and thickness The percentage weight variation for all the formulations is tabulated in table---. all the tablets passed weight variation test as the % weight variation was within the USP pharmacopoeia limit ±7.5%. The weight of all the tablets was found to be uniform. The thickness of tablets was measured by using vernier caliper by picking the tablets randomly. The values are almost uniform in all formulations. Thickness was found in the range from 3.17 to 3.19 mm respectively

Hardness and Friability The hardness test was performed by Monsanto tester. Hardness was maintained to be within 2.3 kg/cm^2 to 2.4 kg/cm^2, as these tablets are rapidly disintegrating. The lower standard deviation values indicated that the hardness of all the formulations were almost uniform and posses good mechanical strength with sufficient hardness. The study results are tabulated in table was well within approved range(<1%) in all tablet formulations results revealed that the formulated FDT posses good mechanical strength.

Disintegration test Tablets disintegrates within 1minutes.

***In vitro* dissolution studies** All six formulations were subjected for the in vitro dissolution studies using tablet dissolution tester USP with a rotating paddle stirrer at 50 rpm and 37^0C± 0.5^0 C. A sample of dissolution fluids were withdrawn through a pipette at different time intervals and were assayed at 225nm for Atenolol drug content using a UV/ visible spectrophotometer. The in vitro release rates were showed in figure no.7.9 and this dissolution data was further treated for compression between all the formulations. Cumulative % drug release was calculated on the basis of mean Atenolol present in respective formulation. The rapid drug dissolution observed in formulation F1 and F2 i.e. 97.0% and 99.88% respectively at the end of 15 minute. On the other hand in formulations F3and F4 release 96.2% and 98.2% respectively at the end of 15 minute and in Formulations F5 and F6 release 96.9% and 98.0% respectively at the end of 15 minute. The rapid dissolution in formulations F2 might be due to fast break down of particles and rapid absorption of drug.

Table 1: Composition of Orally Disintegreting Tablets of Atenolol

S. No.	Materials	F1	F2	F3	F4	F5	F6
1.	Atenolol	25	25	25	25	25	25
2.	Cyclodextine	25	25	25	25	25	25
3.	Lactose(Spray Dried)	96	86	96	86	96	86
4.	MCC	40	40	40	40	40	40
5.	Crospovidone	10	20	-	-	-	-
6.	Croscarmellose sodium	-	-	10	20	-	-
7.	Sodium startch glycolate	-	-	-	-	10	20
8.	Aspartame	2	2	2	2	2	2
9.	Aerosil	1	1	1	1	1	1
10.	Mg Stearate	1	1	1	1	1	1
	Total	200(mg)	200(mg)	200(mg)	200(mg)	200(mg)	200(mg)

Table 2: %Drug Release study of Formulated tablets of Atenolol

Time (min)	% Cumulative drug release					
	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0
2	22.1	23.0	19.2	22.9	20.3	22.0
4	50.0	51.3	42.2	50.1	46.0	50.0
6	70.5	72.5	68.4	73.0	68.2	69.9
8	84.0	85.3	82.1	83.2	78.2	84.2
10	90.1	92.0	90.8	90.0	88.6	92.2
12	96.1	97.9	93.5	94.1	94.2	96.9
15	97.0	99.88	96.2	98.2	96.9	98.0

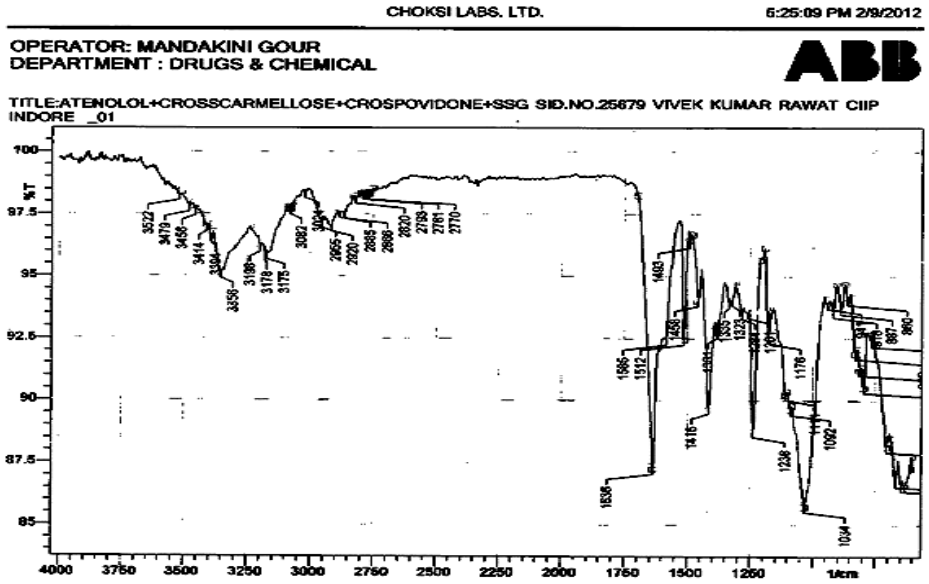

Fig. 1: FT-IR of Atenolol + SSG+ Croscormellose+ Crospovidone spectra

Conclusion

The enhancement of dissolution rate and oral bioavailability of poorly soluble drugs remains one of the most challenging aspects of drug development. Among the various methods of enhancement of the dissolution rate and oral bioavailability, various disintegrating agent was used and successful with a number of drugs. In the present investigation, studies were carried out on enhancement of dissolution rate of Atenolol by forming inclusion complex with β-cyclodextrine. A new class of tablet excipients called " Super Disintegrants" was also used CP gave highest enhancement of dissolution rate and efficiency of Atenolol.The order of enhancement of the dissolution rate with various superdisintegrants was found to be CP >SEG> CCS.

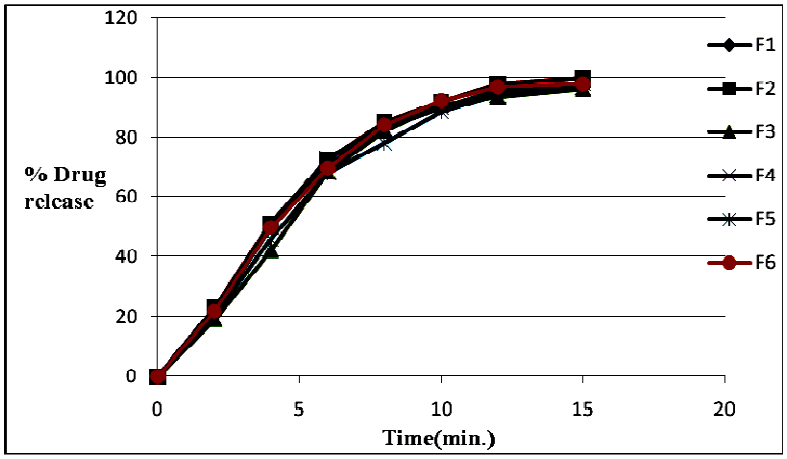

Fig. 2: dissolution Profile

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