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FORMULATION AND EVALUATION OF DELAYED RELEASE TABLETS OF ATENOLOL

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ABSTRACT

Atenolol is a selective β_1 receptor antagonist, a drug belonging to the group of beta blockers (sometimes written β-blockers), a class of drugs used primarily in cardiovascular diseases. Introduced in 1976, Atenolol was developed as a replacement for Propranolol in the treatment of hypertension. The aim of the present study is to develop a pharmaceutically stable, cost effective and quality improved formulation Containing Atenolol. In this study Atenolol delayed release tablets were prepared by using different concentrations of polymers. All the formulations evaluated for optimum release and among all the formulations F6 (86.1%) was found to be best of all the formulations showing drug release matching with the Reference product (84.83%) so to that formulation all the tests were done for conformation.

KEYWORDS

Atenolol, Propranolol, Delayed release and β-blockers.

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INTRODUCTION[1-2]

A Delayed Release dosage form is designed to release the drug at a time other than promptly after administration. Dosage forms can be designed to modify the release of the drug over a given time or after the dosage form reaches the required location.

Delayed Release oral dosage forms can control where the drug is released, e.g. when the dosage form reaches the small intestine (enteric-coated dosage forms) or the colon (colon-specific dosage forms). Delayed Release systems release a bolus of

the drug after a predetermined time in a predetermined location, i.e. they do not release the drug immediately after ingestion, for example enteric-coated tablets, pulsatile-release capsules.

Delayed Release dosage forms are designed to provide spatial placement or temporal targeted delivery of a drug to the distal human gut. Spatial placement relates to targeting a drug to a specific organ or tissue, while temporal delivery refers to desired rate of drug release to target tissue over a specified period of time. The primary aim of using delayed release products is to protect the drug from gastric fluids, to reduce gastric distress caused by drugs particularly irritating to the stomach or to facilitate gastrointestinal transit for drugs that are better absorbed from intestine. Delayed Release products are typically enteric-coated or targeted to the colon.

MATERIAL AND METHODOLOGY

Atenolol, Mannitol, Crospovidone, carbonate anhydrous, Hydroxy Propyl Cellulose, Purified Talc, Calcium Stearate, Zein F 4000 [Regular], Poly (Methacrylic acid-co-ethyl acrylate, Triethyl Citrate, Titanium Dioxide, Isopropyl Alcohol and Purified Water are provided by SIMS College of Pharmacy.

METHODOLOGY[3-5]

Formula for preparation of Core tablet of Atenolol (Table No.1)

Preparation of core tablets

Manufacturing Process Flow Chart

The process showed in Figure No.1.

PROCEDURE

Sifting

Atenolol (# 30 mesh Passed), Crospovidone and. Carbonate Anhydrous were sifted through #60 mesh are collected separately.

Dry mixing

Mixing was done in RMG (4.0 Lt Capacity) for 20 min with impeller slow speed and chopper off.

Granulation

Binder preparation

Hydroxy Propyl cellulose dissolved in purified water to form binder solution. Carbonate Anhydrous also dissolved in Purified water.

Granulation

Binder solution added slowly for 90 sec with chopper off. And then add Alkalising agent solution slowly for 60 sec with chopper off and impeller fast. Then Rinse the vessel and add for 60 sec. Then kneading carried out for 120 sec with chopper slow and impeller fast.

Preformulation Study

Objective /Purpose of Preformulation study

Preformulation testing was an investigation of physical and chemical properties of a drug substance alone and when combined with excipients. It was the first step in the rational development of dosage forms.

Pre-formulation studies on active pharmaceutical ingredients (API), inactive ingredients (Excipients), and their combinations were carried out to serve following purposes:

- To Finalize specifications of active pharmaceutical ingredients (API)
- To Study the compatibility between active and inactive ingredient
- Characterization of reference product.

Scope

The use of Preformulation parameters maximizes the chances in formulating an acceptable, safe, efficacious and stable product.

Preformulation study can divided into two subclasses

API characterization,

Compatibility study

Active pharmaceutical ingredient (API) characterization

These are preliminary characteristics of any substance which is useful in identification of specific material. Following physical properties of API were studied.

Melting Point

146ºC - 148ºC.

Loss on drying

1.0 g of sample of Atenolol was accurately weighed and the powder was kept in a moisture balance apparatus for 5 min. at 85ºC and the moisture content was calculated.

The blend evaluated by the following tests

Angle of repose, Bulk density, Tapped density, Compressibility index and Hausner's ratio. The results are tabulated in the Table No.2.

Solubility

Atenolol is practically soluble in water. To make a clear and thermodynamically stable solution, Solubility studies with different solvents or combination of solvents (water, 0.1N HCl, pH 2.1, 4.5, 5.0, 6.8, 7.2, 8.0) were performed. It is done by Equillibrium Solubility Method (Table No.3).

Drug Excipients Compatibility Studies

The compatibility of drug and formulation components is important prerequisite before formulation. It is therefore necessary to confirm that the drug does not react with the polymers and excipients under experimental conditions and affect the shelf life of product or any other unwanted effects on the formulation. The results were tabulated in the Table No.4.

PROCEDURE

Drug is mixed with excipients in different ratio. These mixtures were kept in a 5ml glass amber colored vials and packed properly. These vials are exposed to 40˚c / 75% RH. Observations for physical appearance are made at zero weeks, 2 week, and 4week, the samples were withdrawn for analysis of following parameter:

RESULTS AND DISCUSSION

The all results are showed in following tables.

Appearance and physical conditions

Sieve Analysis

The procedure involves the Electromagnetic Sieve shaking of the sample through the series of successively arranged sieves (sieve no. - 25, 30, 40, 60, 80,100 and pan weight), and weighing of the portion of the sample retained on each sieve and calculate percentage retained on each sieve.

Evaluation of Core Tablets

The core tablet evaluated for Thickness, Hardness, Friability Test, Weight Variation Test and Dissolution. The results are tabulated in the Table No.5.

The dissolution profiles of Reference product shown in the Table No.6.

The dissolution profiles of all the formulations showed in the Table No.7 and Figure No2 and 3.

Dissolution Parameters

Medium : 0.1N HCl (Degassed) - for 2 hours and 6.8 phosphate buffer (Degassed) for 45 minutes.
Apparatus : Apparatus- I
Quantity : 900 mL
RPM : 100
Temperature : 37 ± 0.5°C
Time : 2 hours and then every 1 hr.

Table No.1: Formula

S.No	Ingredients(mg)	F 1	F2	F3	F4	F5	F6	F7	F8	F9
1	Atenolol	95	95	95	95	95	95	95	95	95
2	Mannitol	85	83	81	79	79	77	78	79	76
3	. Carbonate Anhydrous	6	6	6	6	6	6	6	6	6
4	Hydroxy Propyl cellulose	2	4	6	4	4	4	4	4	4
5	Cross Povidone	8	8	8	10	12	14	13	12	14
6	Calcium Stearate	2	2	2	2	2	2	2	2	3
7	Purified Talc	2	2	2	2	2	2	2	2	2
8	Purified Water	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s
Total		200	200	200	200	200	200	200	200	200

Table No.2: Blend Properties of Formulations of Core Tablet

S.No	Formulation	Blend Characterization				RESULT
		B.D (gm/ml)	T.D (gm/ml)	C.I (%)	H.R	
1	**F1**	0.69	0.94	26.59	1.3	Poor Flow
2	**F2**	0.68	0.84	19.04	1.23	Fair
3	**F3**	0.68	0.86	20.93	1.26	Fair
4	**F4**	0.64	0.79	18.98	1.23	Fair
5	**F5**	0.65	0.78	16.66	1.20	Fair
6	**F6**	0.64	0.80	20.00	1.25	Fair
7	**F7**	0.61	0.71	13.58	1.15	Good
8	**F8**	0.60	0.69	12.24	1.13	Good
9	**F9**	0.59	0.68	13.23	1.15	Good

Table No.3: Properties of Atenolol

S.No	Parameter	Atenolol
1	Organoleptic Evaluation	Atenolol is a white to off-white crystalline powder
2	Solubility Analysis	Freely soluble in water and ethanol.

Table No.4: Result of Compatibility Study

S.No	Name of the Excipient	Ratio	Initial	Final observation		Conclusion
				40°C/75% RH		
				2nd week	4th week	
1	Atenolol		White to off white	White to off white	White to off white	Compatible
2	Atenolol : Cross povidone	1 : 1	white	white	white	Compatible
3	Atenolol : HPMC	1 : 1	White to off white	White to off white	White to off white	Compatible
4	Atenolol : Methacrylic acid co polymer	1 : 5	white	white	white	Compatible
5	Atenolol : Mannitol	1 : 5	white	white	white	Compatible
6	Atenolol :Povidone k 30	1 : 1	white	Off white	Off white	In Compatible
7	Atenolol: Carbonate Anhydrous	1 : 1	white	white	white	Compatible
8	Atenolol : SLS	5 : 1	white	Off white	Light brown	In compatible
9	Atenolol : Titanium dioxide	5 : 1	white	white	white	Compatible
10	Atenolol : Tri ethyl Citrate	5 : 1	white	white	white	Compatible
11	Atenolol : Propylene glycol	20 : 1	white	Off white	Brown	In Compatible
12	Atenolol : Meglumine	1 : 1	white	yellow	yellow	In compatible
13	Atenolol : pregelatinised starch	1 : 5	white	brown	brown	In compatible
14	Atenolol : Hydroxyl propyl cellulose	1 : 1	white	white	white	Compatible
15	Atenolol : talc	3 : 1	white	white	white	Compatible

16	Atenolol : Magnesium Stearate	3 : 1	white	Off white	Off white	In Compatible
17	Atenolol : Zein	1 : 1	yellow	yellow	yellow	Compatible
18	Atenolol : Calcium Stearate	3 : 1	white	white	white	Compatible
19	Atenolol : beta cyclo dextrin	1 : 1	white	Off white	yellow	In compatible
20	Atenolol : Ethyl cellulose	1 : 5	white	Pale yellow	Pale yellow	In compatible

Table No.5: Physical Evaluation (Core tablets)

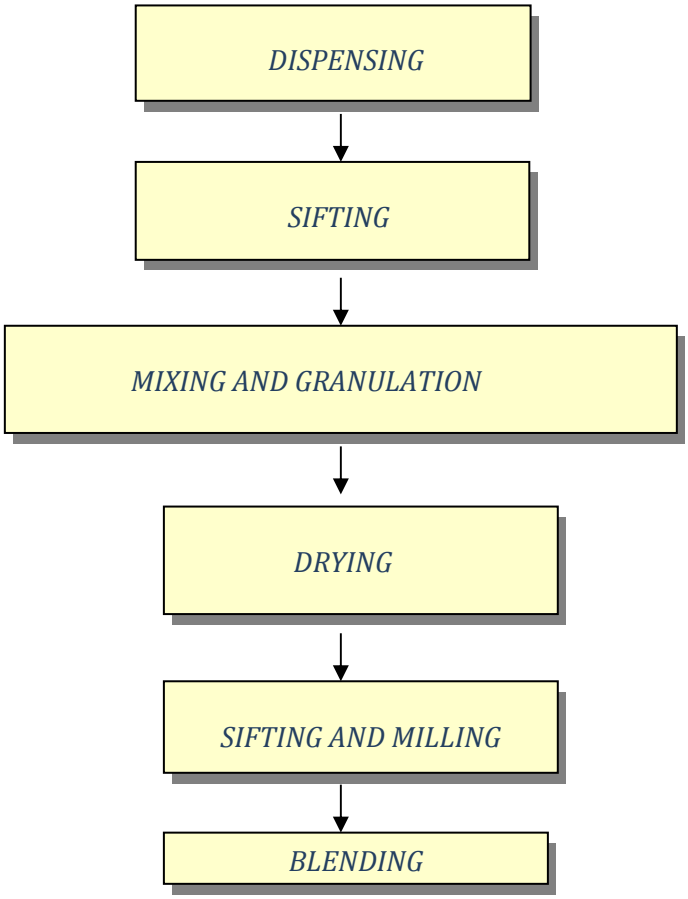
S.No	Physical parameter	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	Weight variation	200±0.5	200±1.0	200±1.0	200±1.0	200±0.5	200±0.5	200±0.5	200±0.5	200±0.5
2	Hardness	12.5	12.2	12.6	12	12.1	12.2	12	12.3	12
3	Thickness (mm)	3.54	3.54	3.53	3.53	3.54	3.54	3.54	3.54	3.53
4	Friability	0.9	0.4	0.6	0.4	0.43	0.42	0.34	0.32	0.36

Table No.6: Cumulative % Drug release (reference product)

S.No	Unit/ time hrs	Unit 1	Unit 2	Unit 3	Unit 4	Unit 5	Unit 6	Average
1	0	0	0	0	0	0	0	0
2	1	5	8	5	4	8	7	6.16
3	2	8.1	9.0	8.1	5.1	9.5	8.6	8.4
4	3	15.6	16.2	15.5	12.2	15.2	15.4	-
5	4	22	24	34	30	24	31	27.5
6	5	32.4	30	35	35	30	35	-
7	6	38	36	37	38	35.2	37.1	-
8	7	44	48	52	49	42	51	47.66
9	8	49	49.1	53	52.1	49.8	52.4	-
10	9	56	58	62	61	55	59	58.5
11	10	58.1	59.2	63.2	62	55.9	60	-
12	11	66	65	64	69	70	64	66.33
13	12	84	88	72	88	89	88	84.83

Table No.7: Dissolution profiles of all formulations

S.No	Time hrs	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	0	0	0	0	0	0	0	0	0	0
2	1	8.2	9.1	8.2	8.5	9.5	6.12	9.16	8.6	8.9
3	2	15.2	13.5	12.5	10.9	15.6	8.52	16.9	12.5	11.9
4	3	16.16	14.9	16.9	13.7	17.16	15	25.1	15.9	12.8
5	4	35.2	34.8	28.2	22.8	34.5	26.96	29.4	32.6	21.9
6	5	42.7	39.1	35.2	29.5	42.7	32.8	32.83	40.8	28.5
7	6	54.1	50.9	39.3	36.7	50.1	36.4	42.8	51.2	36.7
8	7	60.83	65.2	40.7	43.16	62.15	46.9	49.62	66.5	42.5
9	8	71.6	69.1	46.2	45.2	70.1	51	58.66	69.1	45.2
10	9	79.4	74.8	51	49.6	79.4	58.4	65.12	75.6	50.6
11	10	85.4	83.4	62.5	70.1	82.6	58.9	70.15	78.2	69.1
12	11	92.1	92.8	69.4	79.2	94.1	65.8	89.5	90.8	80.1
13	12	96.63	96.16	78.1	89.1	96.63	86.1	95	95.16	89.2



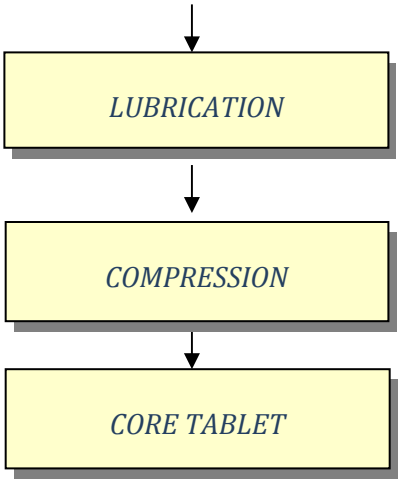


Figure No.1: Manufacturing Process Flow Chart

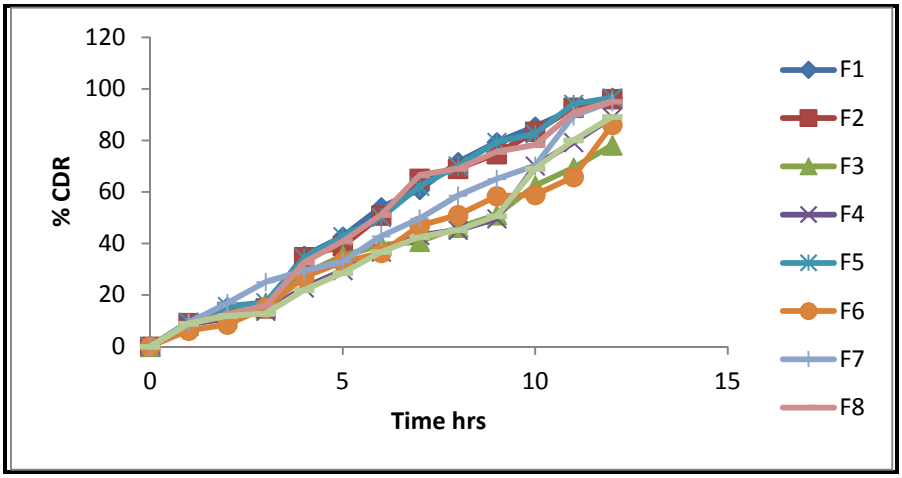


Figure No.2: Dissolution profiles of all formulations

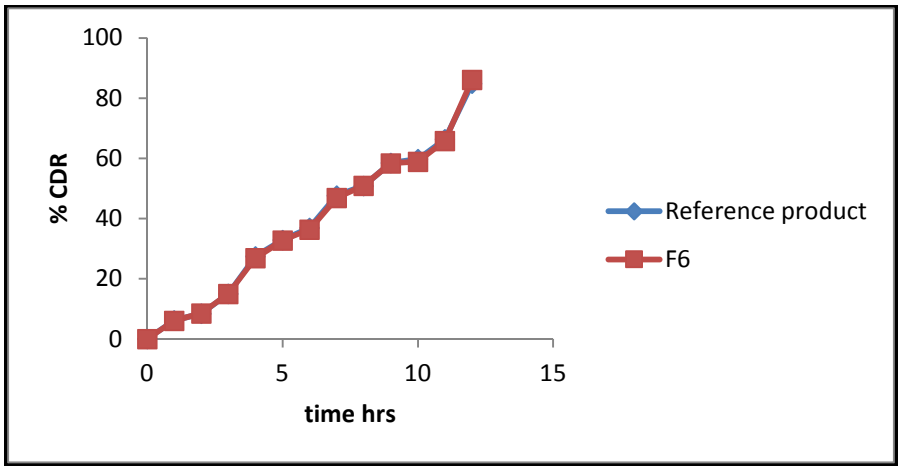


Figure No.3: Comparison between reference product percent CDR vs. F6 Formulation % CDR

CONCLUSION

Core tablets were prepared with different concentrations of binder, lubricant, Disintegrant and found the physical parameters and from that have optimized the concentration of binder, lubricant, disintegrant and formulated the core tablet by using wet granulation method due to its poor flow properties. To that core tablet barrier coating was given up to 1.5 % weight build up and then they are enteric coated with initially 15 %. And then by increasing the enteric coating build up for different formulations, finally compared the dissolution with Reference product. The formulated tablets were evaluated. Weight variation, hardness, friability tests were performed. In-vitro release of drug was studied for all the formulations. Formulations containing tablets compressed with lower hardness shows faster drug release and with optimum hardness it is showing similar profile as that of reference product. The optimum hardness tablets is coated with increasing concentration and observed that at 21 % of coating is matching the dissolution profile of reference product. F6 was found to be best of all the formulations showing drug release matching with the Reference product so to that formulation all the tests were done for conformation.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

REFERENCES

1. Thomas N. Tozer, Malcolm Rowland. Introduction to Pharmacokinetics and Pharmacodynamics, 3rd edition, 2009, 106.
2. Ijeoma F. Uchegbu, Andreas G. Schatzlein. Polymers in Drug Delivery, 13(2), 2016, 221-235.
3. Thomas W Y L, Robinson J. The Science and Practice of Pharmacy, *Lippincott, William and Willins*, 20th edition, 1999, 903-911.
4. Lee T W Y, Robinson J R. Remington: The science and practice of pharmacy, *Lippincott Williams and Wilkins, Maryland*, 20th edition, 2000, 1069-1070.
5. William Andrew. Pharmaceutical Manufacturing, Encyclopedia, 3rd edition, Volume 1.
6. Wise, Donald L. Handbook of Pharmaceutical Controlled Release Technology, 10(6), 2000, 473-486.
7. Vasudev S C, Chandy T and Sharma C P. Development of chitosan/polyethylene vinyl acetate co-matrix: controlled release of aspirin heparin for preventing cardiovascular thrombosis, *Biomaterials*, 18(5), 1997, 375-381.
8. Chein Y W. Novel drug delivery systems, In: chein Y W. Oral drug delivery and delivery systems, Marcel Dekker, New York, 1st edition, 1992, 139-196.
9. Vyas S P, Khar. Controlled drug delivery: concepts and advances In: Vyas S P, Khar, eds.controlled oral administration, *Vallabh Prakashan, Delhi, India*, 19th edition, 2002, 155-195.

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