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DEVELOPMENT AND EVALUATION FOR TABLET-IN CAPSULE OF NEFEDIPINE AND ATENOLOL

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Research Article

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ABSTRACT

Delayed drug delivery system (DDS), zero-order DDS, and site-specific DDS are focuses of oral controlled-release solid dosage forms for researchers. Oral delayed DDS, which releases drugs after a programmable period of time, is intended for the therapy of diseases that depend on circadian rhythms. The system consists of a core and a coating. The core is coated with different polymeric barriers by film or compression, and the coating prevents drug release from the core until the polymeric shell is completely swollen or eroded. Better patient compliance and large surface area in the gastrointestinal tract are the two most important advantages of oral drug delivery systems. Zero-order drug delivery systems are designed by researchers assuming that physiological processes and biological functions display constancy over time. Therefore, many efforts have been devoted in the past in developing the drug delivery systems that maintain a better plasma level for an extended period of time.

KEYWORDS: *Tablet in Capsule, Atenolol, Nifedipine, Delayed Drug Delivery System.*

INTRODUCTION

Atenolol is a beta1-selective (cardio selective) beta-adrenergic receptor blocking agent without membrane stabilizing or intrinsic sympathomimetic (partial agonist) activities. In man, absorption of an oral dose is rapid and consistent but incomplete. Approximately 50% of an oral dose is absorbed from the gastrointestinal tract, the remainder being excreted unchanged in the feces. Atenolol, given as a single daily oral dose, was an effective antihypertensive agent providing 24-hour reduction of blood pressure.

Nifedipine is a yellow crystalline substance, practically insoluble in water but soluble in ethanol. Extended-release tablets contain 20 mg of Nifedipine for once-a-day oral administration. Nifedipine selectively inhibits calcium ion influx across the cell membrane of vascular smooth muscle and cardiac muscle without altering serum calcium concentrations. Nifedipine is a peripheral arterial vasodilator which acts directly on vascular smooth muscle. The binding of Nifedipine to voltage-dependent and possibly receptor-operated channels in vascular smooth muscle results in an inhibition of calcium influx through these channels. Nifedipine is completely absorbed after oral administration. The bioavailability of Nifedipine as Nifedipine extended-release tablet relative to immediate release Nifedipine is in the range of 84% to 89%. After ingestion of Nifedipine extended-release tablets under fasting conditions, plasma concentrations peak at about 2.5 to 5 hours with a second small peak or shoulder evident at approximately 6 to 12 hours post dose. The elimination half-life of Nifedipine administered as Nifedipine extended-release tablet is approximately 7 hours.[4]

MATERIALS AND METHODS

MATERIALS

The following materials are received as gifts from JCPL pharmaceutical pvt ltd.: Atenolol and Nifedipine (NP) are active as well as Lactose,PVP-k30,IsoPropyl alcohol (IPA), hydroxyl Propyl Methyl Cellulose k100(HPMC-K100), Sodium carboxy methyl cellulose (CMC),Talc,Mag.stearate ,sodium starch glycolate, sodium lauryl sulphate(SLS), Microcrystalline cellulose (MCC), Dibasic calcium phosphate(DCP).

METHODS

Formula for 1mini-tablet-

INGREDIENT	QTY TAKEN	CATEGORY
Nifedipine	20mg	Active drug
Lactose	21mg	Diluents
Isopropyl alcohol	1ml	Binding solution Exepients
PVP-k30	1mg	
HPMC-k100	20mg	Adhesive polymer
Sod.CMC	24mg	Binding Agent
Talc	2mg	Glident
Magnesium stearate	2mg	Lubricant
Sodium starch glycolate	2mg	Disintegranant
Sod.SLS	2mg	Solubilizing agent
MCC	10mg	Disintegrating agent
Total	**105mg**	

Sustained-release Mini-Tablets (SMTs):

Nifedipine, lactose was mixed and granulated with HPMC solution made by a blend of PVP-K30 and isopropyl alcohol in 1:1 ratio.Then the wet mass was passed through 20# sieve to obtain granules then the granules are dried at 45°C for 4hr. Then the granules obtained were blended with talc, magnesium stearate.and add the remaining ingredient are SLS (Solubulizer), Sodium starch glycolate (Disintegrant), CMC (Binder), and MCC (Disintigrant). The tablets were prepared by direct compression method and then evaluated for weight variation, friability, hardness and dissolution.

Ingredient	NF1	NF2	NF3
Nifedipine	20	20	20
Lactose	31	21	11
Isopropyl alcohol	1	1	1

PVP-k 30	1	1	1
HPMC-k100	10	20	30
Sodium CMC	24	24	24
Talc	2	2	2
Magnesium stearate	2	2	2
Sodium starch glycolate	2	2	2
Sod.SLS	2	2	2
MCC	10	10	10
TOTAL	**105**	**105**	**105**

*All the values taken in Milligram.

Powder plugs with Atenolol:

Accurately weighed quantity of dibasic calcium phosphate (DCP) {65mg} is mixed with the weigh quantity of Atenolol {50mg} the blend is finally mixed with the Pure Talc {30mg}. The prepared mini –tablet was inserted into the capsule body (0 size) the composition of plug is prepared and fill into the body which have already containing the mini-tablet of Nifedipin. The plug fitted snuggly with the wall of the capsule. Finally the capsule cap was placed over the capsule body

EVALUATION STUDY

Weight variation of capsule:

The USP wt variation test is run by weighing 20 capsules individually, calculating the average weight and compared the individual capsule wt to the average weight. The capsule meet the USP test if,no more than two capsule are outside the percentage limit and if no capsule differ by more than two time the percentage limit (± 7.5 %)[6]

Friability test for Mini-tablet:

The friability test was carried out in *Roche Friabilator.*in which the pre weighted 20 tablet placed in the plastic chamber of friabilator that revoles at 25 rpm for 4 min the conventional compressed tablet that loose less than 0.25 to 1% of their wt. are acceptable.

Hardness test for Mini-Tablet:

The hardness test is performed by the *Pfizer tester.*In which the tablet is placed between the two anvils, force is applied to the anvils, and crushing strength just cause the tablet to break is recorded.[6]

Diameter & Thickness for Mini-Tablet:

The Diameter and Thickness are measure by the *verniar caliber scale.* In which permited accurate measurements and provide information on the variation between tablet. The standard value ± 5%. [6]

Dissolution of Mini-Tablet of Nifedipine:
Figure: 1
A. Apparatus No. 1
Medium 900 ml of 0.1 M hydrochloric acid Speed and time. 150 rpm and 120 minutes. Withdraw a suitable volume of the medium and filter. Measure the absorbance of the filtrate, suitably diluted with the Dissolution medium, if necessary, at the maximum at about 340 nm (2.4.7). Calculate the content of $C_{17}H_{18}N_2O_6$ in the medium from the Absorbance obtained from a solution of known concentration of Nifedipine RS in the same medium of dissolution. Not less than 25 per cent and not more than 45 per cent of the stated amount of $C_{17}H_{18}N_2O_6$. (As per IP 2007)

Dissolution of Atenolol Capsule:

In Vitro dissolution studies for all the prepared tablets and the marketed available tablets was carried out using USP paddle method at 50 rpm in 500 ml of 0.1 N HCl (pH 1.2) as dissolution media, maintained at 37 ± 5°C. 5 ml of sample was withdrawn from the dissolution medium at the specified regular intervals, filtered through Whatmann filter paper and assayed spectrophotometrically at 224.2 nm. An equal volume of pre warmed (37°C) fresh medium was replaced into the dissolution medium after each sampling, to maintain the constant volume throughout the test. Then the cumulative percentage of drug release was calculated and represent graphically. **(Figure: 2)**

B. Apparatus No. 1

Medium 900 ml of phosphate buffer pH 6.8 Speed and time. 150 rpm and 6 hours. Withdraw a suitable volume of the medium and filter. Measure the absorbance of the filtrate, suitably diluted with the dissolution medium, if necessary, at the maximum at about 340 nm. Calculate the content of $C_{17}H_{18}N_2O_6$ in the medium from the absorbance obtained from a solution of known concentration of nifedipine RS in the same medium of Medium. Not less than 60 per cent of the stated amount of $C_{17}H_{18}N_2O_6$ (As per IP 2007).

Assay of Nifedipine:

Weigh and powder 20 tablets. Weigh accurately a quantity of the powder containing about 25 mg of Nifedipine, disperse in methanol, shake and dilute to 100.0 ml with methanol, filter. Dilute 20.0 ml of the filtrate to 100.0 ml with Methanol. Measure the absorbance of the resulting solution at the maximum at about 350 nm. Calculate the content of $C_{17}H_{18}N_2O_6$ from the absorbance obtained with a 0.005 percent w/v solution of Nifedipine RS in methanol[7].

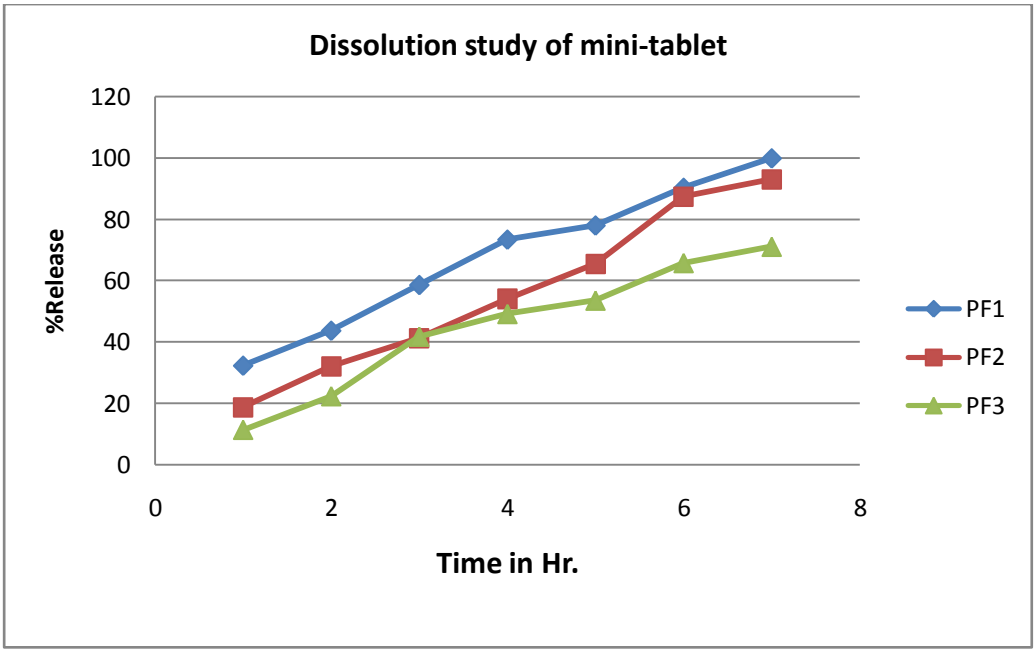
Assay of Atenolol:

Weigh and powder 20 tablets. Weigh accurately a quantity of the powder containing about 0.2 g of Atenolol, transfer to a 500-ml volumetric flask using 300 ml of methanol, heat the resulting suspension to 60°C and shake for 15 minutes. Cool, dilute to 500.0 ml with methanol, filter through a sintered glass funnel (Porosil G3) and dilute a suitable volume of the filtrate with sufficient methanol to produce a solution containing 0.01 percent w/v of Atenolol. Measure the absorbance of the resulting solution at the maximum at about 275 nm. Calculate the content of $C_{14}H_{22}N_2O_3$ taking 53.7 as the value of the specific absorbance at 275 nm[8].

Table:

Test	PF1	PF2	PF3
Hardness	2.1kg/cm2	3.21kg/cm2	3.81kg/cm2
Friability	1.025	0.78%	0.61%
Wt. variation	11%	5.7%	3.2%
Diameter	3.62mm	3.72mm	3.76mm

Figure 1: Dissolution study of Nifedipine* mini tablet

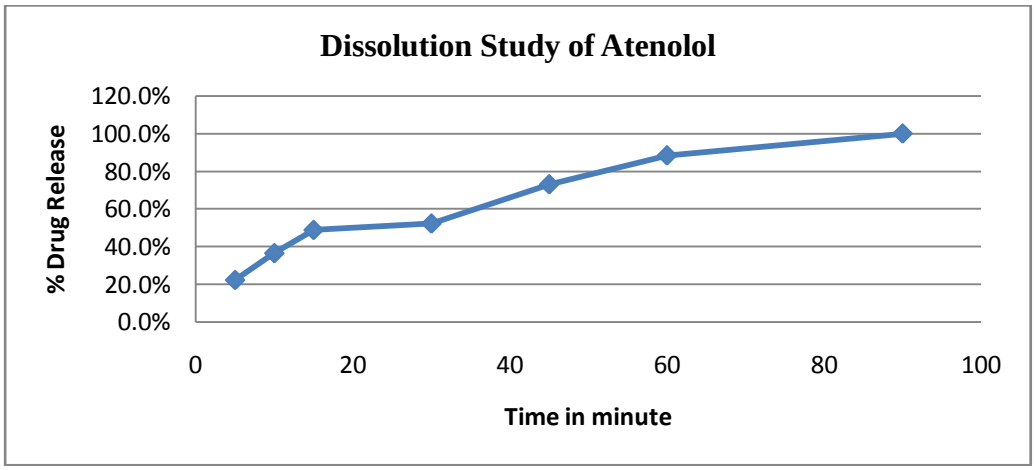


* All experiments were carried out in a dark room, because Nifedipine is highly sensitive to light.

Weight Variation

a)	*Average wt of capsule material:-322mg*
	As per USP specification the no capsule is out of range ±7.5% (i.e. 280.80 to 367.20mg)
b)	*Average wt of filled capsule: - 6.45gm*
	As per USP specification the no capsule is out of range ±2% (i.e. 6.29 to 6.54gm)
c)	*Average wt of content capsule: - 246.90 mg*
	As per USP specification the no capsule is out of range ± 7.5%. (i.e. 231.25 to 268.75)
d)	*Weight of 20 tablets: - 2.09 gm*
	As per USP specification the no capsule is out of range ± 2% (i.e. 2.05 to 2.14 gm)
e)	*e) Average weight of Mini-tablet:-104.9 mg*
	As per USP specification the no capsule is out of range ± 10% (i.e. 94.1 to115.39)

Figure 2: Dissolution study of Atenolol



CONCLUSION

A multifunctional and multiple unit system for oral use are developed by filling versatile mini-tablets in a hard capsule. The aim of the present study was to develop an optimized formula for tablet in Capsule containing Atenolol and Nifedipine for the management of hypertension. Nifedipine was planned to design as the sustained release part and Atenolol as the immediate release part. After preformulation studies it was decided to prepare Atenolol part by free flowing powder and Nifedipine by wet granulation method. For sustained release portion HPMC k100 polymer was used in extragranularly. In the formulation of immediate release sodium starch glycolate and was used as super disintegrant. The free flowing powder of Atenolol was evaluated for weight variation study. The compressed Nifedipine tablets were also evaluated for weight variation, dimension, hardness, friability, drug content, and *in-vitro* drug release. In the above studies NF2 formulation showed promising results. So NF2 formulation was considered as the optimized formulation.

REFERENCES

1. A.C. Ross, R.J. Macrae, Chronopharmaceutical drug delivery from a pulsatile capsule device based on programmable erosion, J. Pharm. Pharmacol. 52 (2000) 903–909.
2. U. Conte, L. Maggi, M.L. Torre, P. Giunchedi, A. La Manna, Press-coated tablets for time-programmed release of drugs, Biomaterials 14 (13) (1993) 1017– 1023
3. S.E. Leucuta, The kinetics of nifedipine release from porous hydrophilic matrices and the pharmacokinetics in man, Pharmazie 43 (12) (1988) 845–848.
4. L. Lachman, H.Liberman, J.Kanig The theory and practice of Industrial pharmacy, third edition 1991 .298-314.
5. Indian Pharmacopia2007 Volume 3, the Indian Pharmacopoeia commission Central Indian Pharmacopoeia laboratory Govt. Of India, ministry of health & family welfare Sector-23, raj Nagar, Ghaziabad 830-831.
6. Indian pharmacopia2007 Volume 2, the Indian Pharmacopoeia Commission Central Indian Pharmacopoeia laboratory Govt. Of India, ministry of health & family welfare Sector-23, raj Nagar, Ghaziabad 130-131.
7. Ranch KM, Koli AR, Vyas BA, Parikh RK, Vyas RB, Maniyar N et al, Formulation, Design and Optimization of Orodispersible Tablets of Atenolol, International Journal of Pharm Tech Research, 2009, 1, 4, 1559-63.
8. United States Pharmacopoeia 30, National Formulary 25, Asian Edition, United states Pharmacopoeial convention Inc., Rockville, 2007, 2647-2648.

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