INTERNATIONAL JOURNAL OF PHARMACY AND ANALYTICAL RESEARCH

ISSN:2320-2831

IJPAR |Vol.6 | Issue 4 | Oct - Dec -2017
Journal Home page: www.ijpar.com

Research article *Open Access*

The effect of superdisintegrants on the dissolution of atenolol fast dissolving tablets

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ABSTRACT

In the present study an attempt has been made to prepare fast dissolving tablets of atenolol, by using different superdisintegrants with enhanced disintegration & dissolution rate. Atenolol is a potent Antihypertensive agent. It competes with sympathomimetic neuro transmitters such as catacholamines such as catecholamines for binding at beta (1) - adrenergic receptors in the heart and vascular smooth muscle, inhibiting sympathetic stimulation. Fast dissolving tablets of atenolol were prepared by using different natural superdisintegrants like fenugreek seed mucilage, Modified Gum karaya and Locust bean gum by direct compression. The precompression blend was tested for angle of repose, bulk density, tapped density, compressibility index and Hausner's ratio. The tablets were evaluated for weight variation, hardness, friability, disintegration time (1 min), dissolution rate, content uniformity, and were found to be within standard limit. It was concluded that the fast dissolving tablets with proper hardness, rapidly disintegrating with enhanced dissolution can be made using selected superdisintegrants. Among the different formulations of atenolol prepared and studied, the formulation F12 containing Locust bean gum was found to be the fast dissolving formulation.

Keywords: Fast dissolving tablets, Atenolol, Superdisintegrant.

INTRODUCTION

The concept of Fast dissolving drug delivery system (FDDDS) emerged from the desire to provide patients with conventional means of taking their medication. Difficulty in swallowing (dysphasia) is a common problem of geriatrics and pediatrics, because of physiological changes associated with these groups of patients. Since the average life span is going–up considerably in this modern era, the number of geriatric patients is growing-up and hence will have significant impact on development of drug delivery systems [1].

Fast dissolving tablet is one of such example, for the reason of rapid disintegration or dissolution in mouth with little amount of water or even with saliva. Significance of this drug delivery system includes administration without water, accuracy of dosage, ease of portability, alternative to liquid dosage forms ideal for pediatric and geriatric patients and rapid onset of action [2].

Superdisintegrants act by swelling and due to swelling pressure exerted in the outer direction or radial direction which causes the tablet to burst or the accelerated absorption of water leading to promote disintegration. Proposed mechanism for the action of disintegrants include water uptake through wicking, swelling, deformation recovery and particle repulsion [3].

Atenolol competes with sympathomimetic neuro transmitters such as catacholamines 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 hypo tension higher doses of atenolol also competitively block beta (2) - adrenergic responses in the bronchial and vascular smooth muscles [4].

MATERIALS AND METHODS

Materials

Atenolol, fenugreek seed mucilage, modified Gum karaya and Locust bean gum were obtained from Yarrow chemicals, Vadodara and all other chemicals/ solvents used were of analytical grade [5-10].

Method

Preparation of atenolol of fast dissolving tablets

All ingredients were triturated individually in a mortar and passed through #60 sieve. Then required quantity of all ingredients were weighed for a batch size of 50 tablets and mixed uniformly in a mortar except talc and magnesium stearate [11-17]. Finally magnesium stearate and talc were added as lubricant. This uniformly mixed blend was compressed in to tablets containing 4mg drug using 5mm flat face surface punches on a cemache rotary tablet machine by direct compression method. Total weight of tablet was kept 100mg[4].

Table No1: Formulations of Atenolol containing different natural superdisintegrants

Ingredients(mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Atenolol	25	25	25	25	25	25	25	25	25	25	25	25
Fenugreek seed mucilage	2	4	6	8	-	-	-	-	-	-	-	-
Gellan gum	-	-	-	-	3	6	9	12	-	-	-	-
Locust bean gum	-	-	-	-	-	-	-	-	5	10	15	20
Mannitol	65	63	61	59	64	61	58	55	62	57	52	47
Aspartame	4	4	4	4	4	4	4	4	4	4	4	4
Magnesium stearate	2	2	2	2	2	2	2	2	2	2	2	2
Talc	2	2	2	2	2	2	2	2	2	2	2	2
Total(mg)	100	100	100	100	100	100	100	100	100	100	100	100

Evaluation of Tablets

The formulations were evaluated for hardness, weight variation, thickness, friability, disintegration time, content uniformity, assay and *in vitro* dissolution study.

Tablet Hardness

Hardness is the crushing strength of tablet which determines the ease of handling and rigors of the transportation. For each formulation, 3 tablets were used for the study. The hardness of the tablet was determined and expressed in Kp.

Weight Variation Test

Weight variation test was done by weighing 20 tablets individually, calculating the average weight and comparing the individual tablet weight to the average. The data presented in **Table 1** clearly show the weight variation tolerance for uncoated tablets.

Thickness

The thickness of the tablets was measured using Digital Vernier Caliper, and expressed in mm.

Friability

Friability test is performed to assess the effect of friction and shocks, which may often cause tablet to chip, cap or break. Roche friabilator was used for the purpose. This device subjects a number of tablets to the combined effect of abrasion and shock by utilizing a plastic chamber that revolves at 25 rpm dropping the tablets at distance of 6 inches with each revolution. Preweighed sample of tablets were placed in the friabilator, which was then operated for 100 revolutions. Tablets were dedusted and reweighed.

The percent friability was measured using the formula:

$\%F = \{(W - W_0)/W_0\}*100$

Where, %F = Friability in percent,

W = Initial weight of tablet.

W_0 = Weight of tablet after test.

Disintegration Time

One tablet was placed in each of six tubes of disintegration test apparatus. Disintegration test was carried out at 37 ± 2 ^{0}C according to USP XXII., Disintegration test apparatus without disc, time required for complete passage of tablet fragments through the sieve (#10) was considered as a disintegration time of a tablet.

Assay

For this, 30 tablets were randomly selected from all formulations. Out of 30 tablets 10 tablets were crushed into fine powder. The powder taken equivalent to label claim was weighed accurately, dissolved in their respective media and assayed individually at respective λ max against the reagent blank. The drug content should be within 90% to 110% of the labeled claim.

Uniformity of content

One tablet was powdered, shaken with 1 ml of dilute HCl and 40 ml of water for 15 min, and added sufficient water to produce 100 ml and mixed well. Centrifuged about 15 ml and to 10 ml of the clear, supernatant liquid 2 ml of 1M HCl and sufficient water were added to produce a solution containing about 0.005 % w/w concentrated HCl. The absorbance of the resulting solution was measured at the λmax. of 228 nm. Then the content corresponding to atenolol in the tablet was calculated.

In vitro Dissolution studies

The *in vitro* dissolution study was carried out in USP dissolution test apparatus Type 2 (paddle). Samples were withdrawn at 1, 2, 4, 6, 8, and 10 minutes time intervals by replacing with same dissolution medium and the dissolution of the drug was expressed as percentage drug dissolved by using following formula.

$$\%\ \text{Drug Release} = \frac{\text{Sample Abs}}{\text{Std Abs}} \times \frac{\text{Wt of Std}}{\text{Bath Volume}} \times \text{D.F} \times \frac{\text{Bath volume}}{\text{Amt. of drug}} \times \text{D.F} \times \frac{\text{Potency}}{100} \times 100$$

RESULTS & DISCUSSIONS

Table 2: Atenolol tablets characterization

Formulation code	Weight variation	Thickness (mm)	Hardness (kg/cm^2)	Drug Content	Disintegration Time (Sec)	Water Absorption Ratio
F1	98.6±0.5	2.4±0.06	2.92±0.06	94.4	90	49.42
F2	100.1±0.4	2.3±0.03	2.87±0.05	90.5	71	56.53

F3	100.4±0.1	2.4±0.05	2.83±0.04	92.9	82	69.82
F4	101.1±0.2	2.4±0.02	2.98±0.08	93.9	51	80.56
F5	99.5±0.3	2.4±0.07	3.06±0.03	95.3	79	83.30
F6	99.1±0.7	2.2±0.08	2.9±0.02	92.96	92	43.97
F7	99.6±0.8	2.4±0.09	2.94±0.08	94.99	58	61.94
F8	100.8±0.3	2.4±0.02	2.97±0.09	98.2	70	84.46
F9	99.4±0.5	2.3±0.04	3.01±0.07	96.12	49	56.78
F10	99.7±0.4	2.4±0.07	3.13±0.05	98	70	66.54
F11	100.1±0.2	2.4±0.03	2.98±0.08	93.41	75	72.35
F12	99.6±0.5	2.3±0.07	2.93±0.02	99.58	43	86.98

Values are expressed as Mean ±SD, n=3

In the present study Atenolol Fast dissolving tablets were prepared by using superdisintegrants namely, gellan gums, locustbeangum, fenugreekseed mucilages. All the formulations were evaluated for various parameters like hardness, friability, drug content, disintegration time and *In-vitro* drug release values are given in Table No. 2.

The hardness of the tablets was found to be 2.4 + 0.10 to 2.6 + 0.057 kg/cm^2 and friability was found to be below 1% indicating good mechanical resistance. The thickness of the tablets was found to be 2.1± 0.057 to 1.2± 0.04. All the tablets passed weight variation test, as percentage weight variation was within the pharmacopoeial limits i.e. ±7.5%. The drug content was found to be 98.02 to 99.89%, indicating uniform distribution of drug in tablets.

Invitro dissolution studies

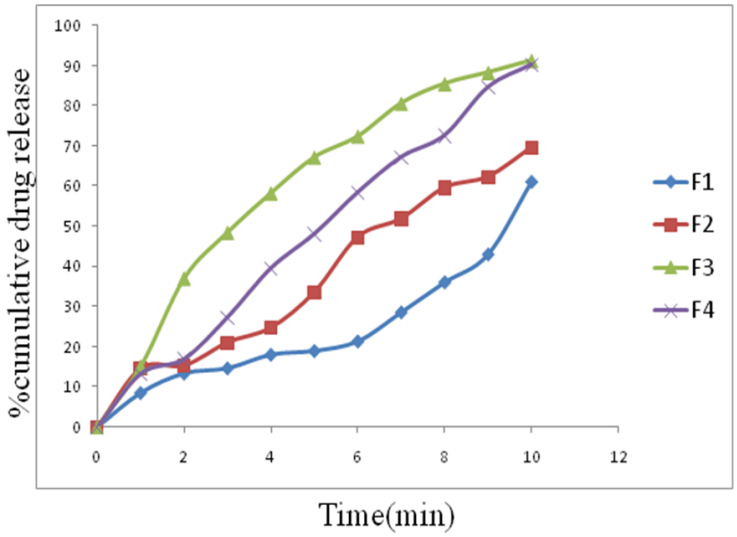

Fig no: 1 *In vitro* drug releases of F1, F2, F3 and F4 formulations

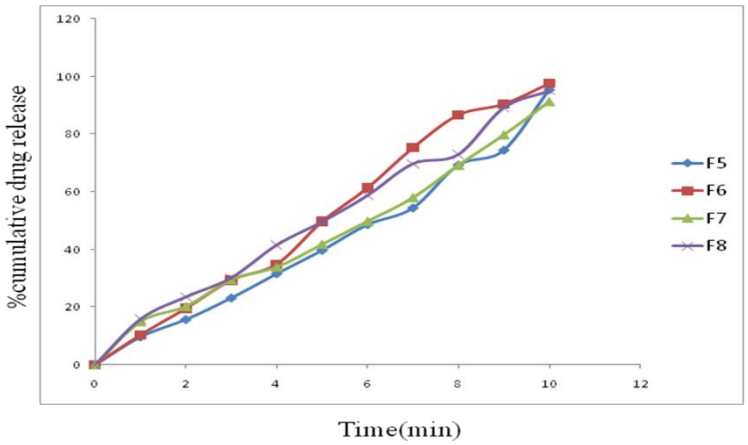

Fig no: 2 *In vitro* dissolution graph for F5-F8

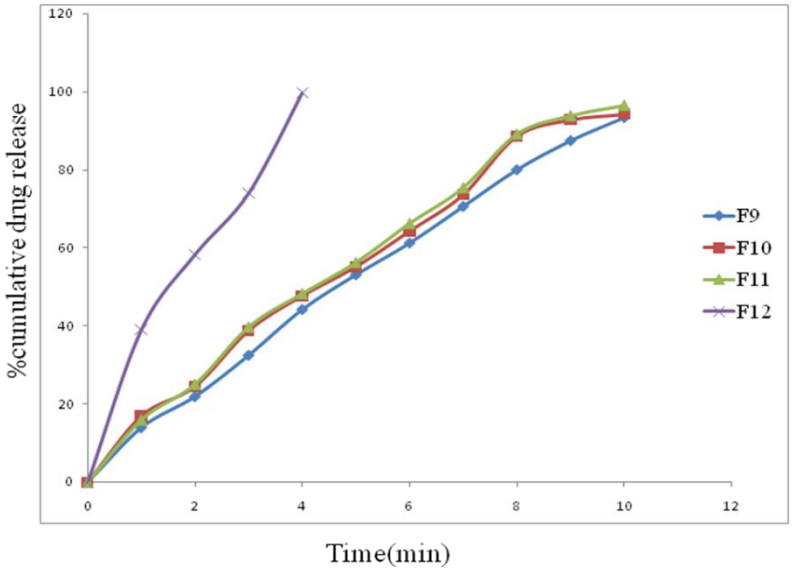

Fig no: 3 *In vitro* dissolution graph for F9-F12

CONCLUSION

Fast dissolving tablets of atenolol were prepared by using different natural superdisintegrants like fenugreek seed mucilage, Modified Gum karaya, Locust bean gum by direct compression. Precompression parameters were conducted for all formulations blend and were found to be satisfactory. The prepared tablets were evaluated for various parameters like content uniformity, hardness, friability, wetting time, water absorption ratio, disintegration time and *in –vitro* dissolution. The results indicated that the tablets complied with the official specifications. The disintegration studies shown that the all formulations disintegrated in less than 140 seconds. The formulation F12 shown less disintegration time of the fenugreek seed mucilage and gellan gum shown more disintegration time than Locust bean gum. Accelerated stability studies on optimized formulation were performed. The formulation was found to be stable; there was no change in the hardness, friability, disintegration time, and *in -vitro* drug release pattern. In conclusion, it can be stated that the objective of the study has been achieved. From the above study the formula used F12 formulations was concluded as an optimized formulation due to its less disintegration time and good % drug release (99.42%) when compared with other formulations

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