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M Prashanthievangelin
Southern Institute of Medical Sciences, Guntur, Andhra Pradesh, India

P Prem Kumar
Southern Institute of Medical Sciences, Guntur, Andhra Pradesh, India

SK Zakeer
Southern Institute of Medical Sciences, Guntur, Andhra Pradesh, India

G Sai Chandrasekhar
Southern Institute of Medical Sciences, Guntur, Andhra Pradesh, India

B Pravallika
Southern Institute of Medical Sciences, Guntur, Andhra Pradesh, India

G Radhika
Southern Institute of Medical Sciences, Guntur, Andhra Pradesh, India

Corresponding Author:
M Prashanthievangelin
Southern Institute of Medical Sciences, Guntur, Andhra Pradesh, India

Formulation and evaluation of atenolol oral dispersible tablets by using different super Disintegrants

M Prashanthievangelin, P Prem Kumar, SK Zakeer, G Sai Chandrasekhar, B Pravallika and G Radhika

Abstract
Novel Drug Delivery System oriented towards increasing safety and efficacy of existing drug molecule through novel concepts like oral drug delivery system. therein the essential approach utilized in the event of the oral dispersible tablets by using different super disintegrants. Another approach utilized in developing oral dispersible tablets is maximizing pore structure of the tablets. Freeze-drying and vacuum-drying techniques are tried by researchers to maximise the pore structure of tablet matrix. Tablets containing Atenolol with super disintegrants like Starch citrate, Sodium starch glycolate and cross carmellose sodium were prepared by direct compression technique. The tablets were evaluated for percentage friability, wetting time, disintegration time and in vitro studies etc.

Keywords: Atenolol, superdisintegrants, oral dispersible tablets, direct compression technique and *in vitro* studies

Introduction
The conventional dosage forms (tablet and capsule) have wide acceptance up to 50-60 you look after the entire dosage forms. Tablet remains hottest dosage form existing forms existing due to simple self-administration, compact in nature, easy to manufacture and it are often delivered in accurate dose. One drawback of solid dosage form is difficulty in swallowing (dysphasia) and chewing in some patients particularly in geriatric and paediatric patients. the matter of choking is common phenomenon in geriatric patients thanks to fear of choking, hand tremors, dysphasia [1]. Orally disintegrating tablets also are called as Or dispersible tablets, quick disintegrating tablets, mouth dissolving tablets, fast disintegrating tablets, fast dissolving tablets, rapid dissolving tablets, porous tablets, and rap melts [2]. However, of all the above terms, us pharmacopoeia (USP) approved these dosage forms as ODTs. Recently, European pharmacopoeia has used the term or dispersible tablet for tablets that disperses readily 2 and within 3 min in mouth before swallowing . An orally disintegrating tablet or or dispersible tablet (ODT) may be a drug dosage form available for a limited amount of over-the-counter (OTC) and prescription medications. ODTs differ from traditional tablets there in they're designed to be dissolved on the tongue instead of swallowed whole. The ODT is an alternate dosage form for patients who experience dysphasia (difficulty in swallowing) or for where compliance may be a known issue and thus a neater dosage form to require ensures that medication is taken. a further reason to use ODTs is that the convenience of a tablet which will be taken without water [3].

Materials and Methods
Atenolol was obtained from Zudus Cadila Health Care Pvt.Ltd, India. Starch citrate, Sodium starch glycolate, Cross carmellose sodium, Mannitol, Micro crystalline cellulose, Talc and Magnesium Stearate were purchased from Qualigens fine chemicals, Mumbai, India. All other chemicals and ingredients were used for study are of Analytical grade.

Methods
spectra of the pure drug, super disintegrants and formulations were recorded by using BOMEN MB SERIES FTIR instrument. Approximately 5mg of samples were mixed with 50mg of spectroscopic grade KBr, samples were scanned within the IR range -1 -1 from 500 to 3500 cm, with a resolution of 4 cm. Pre-compression studies of Oral dispersible tablet powder Bulk density 3 gm of powder were weighed separately and transferred into 100ml measuring cylinder, initial volume was measured and calculated according to the formula

Formula
Bulk density = Mass / Volume T apped density
Tapped density is decided by placing a graduate containing a known mass of powder and mechanical tapper apparatus, which is operated for a hard and fast number of taps until the powder bed volume has reached a minimum volume. Using the load of the powder within the cylinder and this minimum volume, the tapped density could also be computed [4].

Formula
Tapped density = Weight of Powder/ Tapped volume of Powder [5].

Angle of Repose
The manner during which stresses are transmitted through a bead and therefore the beads response to applied stress are reflected within the various angles of friction and response. the foremost commonly used of this in angle of repose, which can be determined experimentally by number of methods. the tactic wont to find the angle of repose is to pour the powder a conical on A level , flat surface and measure the included angle with the horizontal [6].

Formula
Preparation of Oral Dispersible Atenolol Tablets
Weigh accurate required amount of Atenolol and every one ingredients. Then mix them in stoichiometric proportions. Then punch the tablets by using tablet punching machine by direct compression technique, as shown in Table No.1.3-6 [7].

Evaluation Parameters
Pre-formulation Studies
Fourier Transform Infrared Spectroscopy
The Fourier transform infra-red analysis was conducted for the structure characterization. FTIR
Available online: www.uptodateresearchpublication.com
θ = Tan-1 (h/r) θ = Angle of repose,
h = Height of the powder cone,
r = Radius of the powder cone.
Compressibility Index or Carr' s Index
Carr's Index is measured using the values of bulk density and tapped density [8].

The following equation is used to find the Carr's Index,

$$CI = \frac{(TD-BD)}{TD} \times 100$$

Where
TD = Tapped density
BD = Bulk density.
Hausner's Ratio
It indicates the flow properties of the powder and ratio of Tapped density to the Bulk density of the powder.
Formula
Hausner's Ratio = Tapped density/Bulk density
Post compression studies of Atenolol Oral dispersible tablets
Hardness or Crushing strength Test Hardness of the tablet decided using the Monsanto hardness tester (The lower plunger was placed in touch with the tablet and a zero reading was taken. The plunger was then forced against a spring by tuning a threaded bolt until the tablet fractured. because the spring was compressed a pointer rides along a gauge within the barrel to point the force. The force required to interrupt the tablet is measured in kilograms and a crushing strength of 4 Kg is typically considered to be the minimum for satisfactory tablets. Oral tablets normally have a hardness of 4 to 10 kg; however, hypodermic and chewable tablets have a hardness of three kg and a few sustained release tablets have a hardness of 10 -20 kg
.
Thickness Test
The thickness of the tablet is usually associated with the tablet hardness are often uses as initial control parameter. Ten tablets were randomly selected from each tablet thickness decided employing a Venire caliper and therefore the reading was recorded in millimeters. Friability Test
The pre-weighed tablets were placed within the friabilator (EF-2, Electro lab, Mumbai) which was then operated for 100rpm, then dusted and reweighed. the traditional compressed tablets that lose but 0.5-1.0% of their weight are generally considered acceptable.

$$I–F \text{ Friability index} = \frac{}{I} \times 100$$

Where,
I - Initial weight
F - Final weight
Weight variation test
Weights of 20 individual tablets were noted and their mean weight also calculated. The percentage deviation was calculated by using the following formula,
Percentage deviation = [X- */ X] × 100
X - Actual weight of the tablet
X *- Average weight of the tablet
Estimation of Drug ContentAn accurately weighed amount of powdered
Atenolol (100 mg) was extracted with water and thesolution was filtered through 0.45 µ membrane filter paper. The absorbance was measured at 228 nm after suitable dilution.

Calculation
The amount of Atenolol present in tablet can be calculated using the formula

At/As x Sw/100 x 100

Where,
At = Absorbance of sample preparation
As = Absorbance of Standard preparation
Sw = weight at Atenolol working standard (mg)

Disintegration time study
Tablet was put into 100 ml distilled water at 37 ± 0 2 C. Time required for complete dispersion of a tablet was measured with the assistance of digital tablet disintegration test apparatus.
Wetting time and motion study
A piece of tissue folded twice was placed during a small Petri dish (internal diameter = 6.5cm) containing 5 ml of water . A tablet was placed on the paper, and therefore the time for complete wetting of the tablet was measured in seconds.
In vitro drug release studies
The dissolution was administered using rotating paddle method; freshly prepared 0.1N HCl (pH 1.2) (900 ml) was placed in dissolution flask and allowed to get temperature at

37±0.5 °C. The tablets were placed in beaker and rotated with 50rpm for 30minutes. 1 ml of sample was withdrawn at different time intervals (5, 10, 15, 20, 25, 30 mints). After each withdrawal, medium was replaced by equal amount of fresh 0.1N HCl (pH 1.2). The sample were diluted to 10 ml with dissolution medium and used for measurement of absorbance at 228 nm. Before this, add 1 ml of 1% FeCl3 solution thereto. The dissolution data obtained were plotted as percentage drug release versus time.

Results and Discussion

Pre formulation studies

Compatibility studies (Fourier Transform Infrared Spectroscopic studies)The fourier transform infra-red analysis was conducted for the surface structure characterization. FTIR spectrum of the formulated tablets, pure drug and different superdisintegrants was recorded. The tablets were taken during a KBr pellet by using BOMENMB SERIES FTIR instrument. The Fourier Transform Infrared Spectroscopy study reveals that there is no interaction between the various superdisintegrants and pure drug. Then all the functional groups are found within the IR spectrum of pure drug and different super disintegrants. Precompression studies of powders

Bulk density The packing properties of the drugs and their formulations widely depend on bulk density. It has been stated that bulk density values but 31.2gm/cm indicate good flow and values greater3than 1.5 gm/cm indicate poor flow. From the results it are often seen that the majority density values are less3 than 1.2gm/cm. this means good flow characteristics of the powders. Values showed in Table No.2.

Tapped density

From the results it are often seen that the Tapped density values indicate good flow characteristics of the powders. Values showed in Table No.2.

Angle of Repose

Angle of repose is a smaller amount than or adequate to 40° indicates free flowing properties of the powders. However angle of repose is bigger than 40° indicates poor low of fabric . It are often observed that the angle of repose for various batches of the powders is found to0be but 40 , it indicates good flow properties of the powders. Values showed in Table No.2.

Compressibility Index or Carr' s Index

Carr's Index is less than or equal to <10 indicates free flowing properties of the powders. HoweverCarr's Index is greater than <10 indicate poor flow of material. It can be observed that the Carr's Index for various batches of the powders is found to be less than >10; it indicates good flow properties of the powders. Values showed in Table No.1.

Hausner' s Ratio

Hausner's Ratio is less than or equal to 1.069 indicates free flowing properties of the powders. HoweverHausner's Ratio is greater than 1.35 indicates poor flow of material. It can be observed that the Hausner's Ratio for various batches of the powders is found to be less than 1.35; it indicates good flow properties of the powders. Values showed in Table No.1.

Table 1: Preformulation parameters

S.No	Formulations	BulkDensity(gm/cm3)	Tapped Density(gm/cm3)	Angle of Repose(ɵ)	Carr'sIndex(%)	Hausner's Ratio
1	F1	0.276	0.307	21.78	10.09	1.112
2	F2	0.267	0.285	22.99	6.31	1.067
3	F3	0.288	0.310	20.85	7.096	1.076
4	F4	0.294	0.323	20.56	10.09	1.098
5	F5	0.312	0.340	21.51	8.23	1.089
6	F6	0.367	0.398	23.24	7.788	1.084

Hardness Test

The hardness of the tablet various batches were evaluated. The presented batches of the tablets of hardness values are found within limits and it determines good strength of the oral dispersible tablets. Values showed in Table No.2.

Table 2: Results of Stability studies

Formulation	Hardness(kg/cm2)	Friability%	Disintegration Time(seconds)
F1	3.66	0.880	25
F2	3.20	0.880	23
F3	3.18	0.666	21
F4	3.16	0.666	22
F5	3.60	0.880	16
F6	3.16	0.666	19

Thickness Test

The thicknesses of tablets were almost uniform in the all formulations and were found to be in the range of 0.36mm. Values showed in Table No.3.

Table 3: Evaluation of tablets

Formulation	Uniformity of Thickness(cm)	WeightVariation(%)	Drug Content(%)
F1	0.36	99.8	99.6
F2	0.36	99.8	99.7
F3	0.36	99.9	99.6
F4	0.36	99.8	99.6
F5	0.36	99.9	99.8
F6	0.36	99.8	99.7

Friability Test

The oral dispersible tablets friability values are found to be less than 1% in all cases and considered to be satisfactory. Values showed Table in No.2.

Weightvariationtest

All this oral dispersible tablets passed weight variation test as the % weight variation was within the pharmacopoeia limits. The weight of the all tablets was found to be uniform with low standard deviation values. Values showed in Table No.3.

Estimation of Drug Content

Drug ingredients of all the batches are within the acceptable range which shows the proper mixing of drug and excipients. Values showed in Table No.3

Disintegration time study

The disintegration time (D.T) of all formulations is shown in the TableNo.4.

Wetting time study

The wetting time study of all formulations is shown in the Table No.4.

***In vitro* drug release studies**

Among all the batches F5 formulations showed the better dispersible and dissolution of drug (Table No.5-7 and Figure 1-3).Ir profiles in (Figure 4-6)

Table 4: *Drug release time* of Atenolol Tablets F4, F5, F6

Time(mins)	Percentage Drug Dissolved		F3
	F1	F2	
0	0.00	0.00	0.00
5	2.15	2.20	2.52
10	6.72	8.13	9.24
15	17.58	19.24	20.23
20	30.62	35.23	39.12
25	45.98	50.19	56.67
30	62.48	68.38	72.46

Table 5: *In-Vitro* Dissolution data of Atenolol Tablets F4, F5, F6

Time(mins)	Percentage drug dissolved		
	F4	F5	F6
0	0.00	0.00	0.00
5	3.15	3.95	2.49
10	10.87	12.82	9.05
15	22.19	25.93	21.70
20	37.54	43.34	40.83
25	58.19	65.32	60.54
30	78.94	82.58	76.67

Absorbance values

Table 6: Standard calibration curve data of Atenolol in 0.1N Hcl at λmax 275nm

S.no	Concentration(µg/ml)	Absorbance(nm)
1.	0	0.00
2.	2	0.501
3.	4	0.509
4.	6	0.504
5.	8	0.553
6.	10	0.538

Standard calibration curve of Atenolol

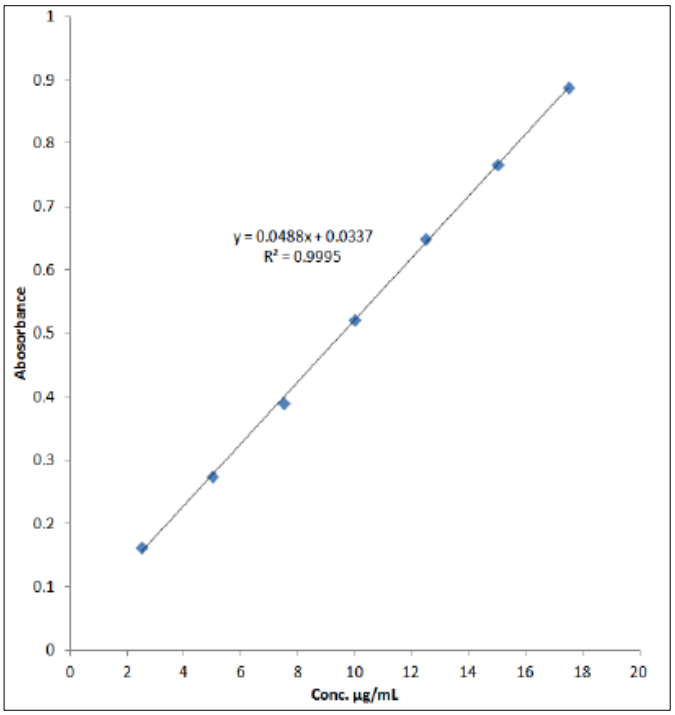

Fig 1: Calibration graph for Atenolol standard at λ275 nm

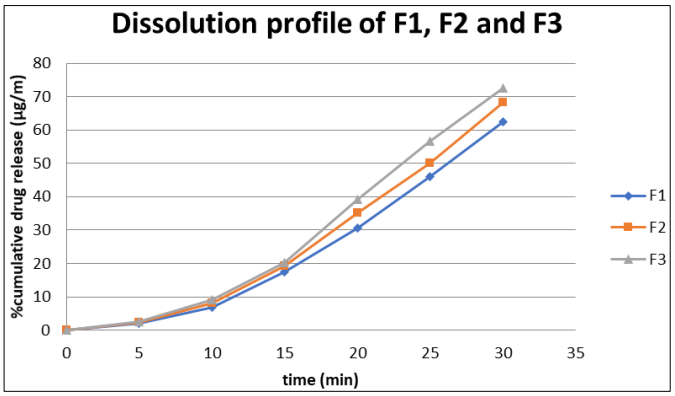

Fig 2: Dissolution profiles of Atenolol tablets of F1, F2, F3

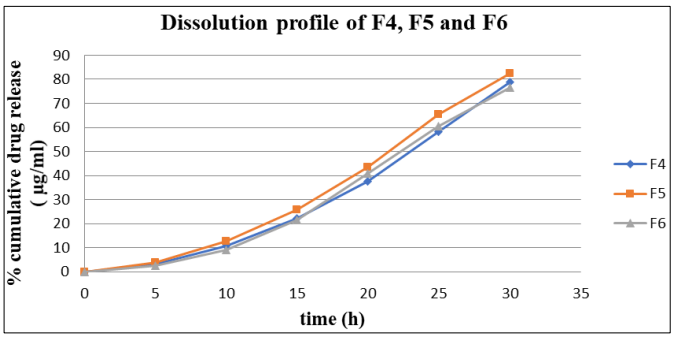

Fig 3: Dissolution Profiles of Atenolol tablets of F4, F5, F6

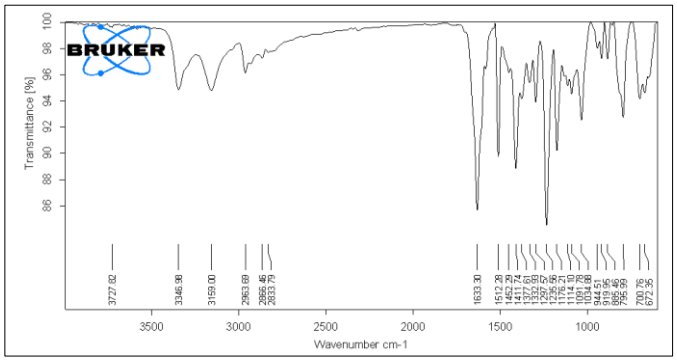

Fig 4: FT- IR Spectra of Atenolol

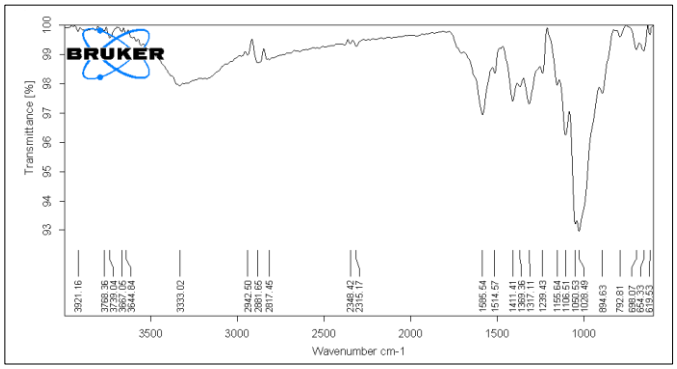

Fig 5: FT- IR Spectra of Atenolol + Crosscarmellose sodium

Conclusion

Oral dispersible tablets of Atenolol were successfully prepared by using different super disintegrants by direct compression method. In the present work the results revealed that the increased proportion of various superdisintegrants were associated with increase in the overall cumulative drug release rate. F5 formulation showed an wetting time of 11 seconds and dispersible time of 16seconds, which was the minimum among all the formulations. *In vitro* dissolution studies showed that the formulation F5 gave the maximum percentagedrug release (82.58%) within 30mins.The combination of cross carmellose sodium and cross povidone (F5) was found to be the best superdisintegrants in the preparation of Oral dispersibletablets of Atenolol. Thus the objective of prepared Atenelol was formulated into fast dissolving tablets was successfully achieved. The formulated fast dissolving tablets of Atenolol may be useful forhypertensive which can improve the patient compliance and hence can minimize the therapeutic response leading to better therapeutic efficacy and safety to the patients.

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