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Formulation And Evaluation Of Oral Fast Dissolving Tablet For Angina

[1]Mr. Anil S. Pathade, [2]Dr. N. N. Bobade, [3]Dr. V. P. Wankhade, [4]Dr. S. C. Atram, [5]Dr. S. D. Pande

[1]Department of Pharmaceutics,

[1]Vidyabharti College of Pharmacy, Amravati, India

Abstract: The present study aimed to develop and evaluate fast-dissolving tablets of atenolol, a cardio-selective beta-blocker, to improve patient compliance and therapeutic efficacy in the management of angina. Atenolol was selected as the model drug due to its low bioavailability (around 50%) and short half-life (6-7 hours). Preformulation studies were conducted to evaluate the physicochemical properties of atenolol. The drug was found to be slightly soluble in water and soluble in organic solvents. Analytical methods were developed for estimation of atenolol using UV-visible spectrophotometry. Fast-dissolving tablets were prepared by direct compression method using different superdisintegrants like croscarmellose sodium, crospovidone, and sodium starch glycolate in varying concentrations. Preliminary, combination, and 32 factorial design batches were formulated and evaluated for pre- and post-compression parameters. The optimized formulation (F5) containing crospovidone (20 mg) showed the fastest disintegration time (44.10 ± 0.31 sec) and maximum cumulative drug release (99.24 ± 0.157% in 10 min). The developed fast-dissolving atenolol tablets are expected to provide rapid onset of action and improved patient compliance in the management of angina.

Index Terms **-** Fast-dissolving tablets, Atenolol, Superdisintegrants, Dissolution kinetics, Patient compliance

I. INTRODUCTION

Oral drug delivery remains the most preferred route of administration due to its convenience, patient acceptability, and cost-effectiveness. However, conventional oral dosage forms like tablets and capsules have certain limitations, especially for geriatric and pediatric patients who may experience difficulty in swallowing (dysphagia). This leads to non-compliance and decreased therapeutic efficacy.

To overcome these issues, pharmaceutical technologists have developed an innovative oral dosage form known as fast-dissolving tablets (FDTs). FDTs, also called orodispersible or mouth-dissolving tablets, are solid dosage forms that disintegrate or dissolve rapidly in the oral cavity within a few seconds, without the need for water [1,2].

Atenolol, a cardio-selective beta-blocker, is widely used in the management of angina pectoris and hypertension. It exhibits low oral bioavailability (around 50%) due to incomplete absorption and extensive first-pass metabolism [3]. Additionally, atenolol has a relatively short half-life of 6-7 hours, necessitating multiple daily dosing. These pharmacokinetic limitations make atenolol a suitable candidate for formulation as a fast-dissolving tablet.

The development of FDTs aims to improve patient compliance, particularly in geriatric, pediatric, and dysphagic patients, by providing a convenient and easy-to-administer dosage form. FDTs also offer advantages like increased bioavailability, rapid onset of action, and reduced first-pass metabolism [4,5].

The present research work focuses on the formulation and evaluation of fast-dissolving tablets of atenolol using various superdisintegrants, such as croscarmellose sodium, crospovidone, and sodium starch glycolate. The objective is to develop a fast-dissolving tablet formulation that can disintegrate rapidly in the oral cavity,

leading to improved dissolution and absorption of atenolol, thereby enhancing its therapeutic efficacy in the management of angina.

II. MATERIALS AND METHODS

Materials:

Atenolol was obtained as a gift sample from Kopran Mumbai., India. Croscarmellose sodium , crospovidone , and sodium starch glycolate (Primojel) were procured from Singlet Mumbai. Microcrystalline cellulose (Avicel PH102), magnesium stearate, and talc were purchased from Glenmark, India. All other chemicals and solvents used were of analytical grade.

Methods:

Preformulation studies: Preformulation studies were performed to evaluate the physicochemical properties of atenolol, such as organoleptic properties, solubility, melting point, and compatibility with excipients using FTIR spectroscopy.

Analytical method development: A simple, accurate, and precise UV-visible spectrophotometric method was developed and validated for the quantitative estimation of atenolol in accordance with ICH guidelines.

Formulation development:

Method of preparation of oral fast disintegrating tablets:

The prepared tablet of each batch was evaluated for the tablet properties. Fast disintegrating tablets of Atenolol were prepared by direct compression method according to the formula given in Table No. 1. Weighed quantity of Atenolol along with different concentration of superdisintegrant and binder along with excipients was mixed in geometric progression in a dry and clean mortar. Then the blend was passed through sieve number 60 for direct compression. The powder blend was then compressed into tablets using a 10 mm punch in multipunch tablet compression machine. These fabricated tablets were evaluated.

Table no.1. Formulation of Preliminary Batches for oral fast Dissolving Tablet

Name of Ingredients	Formulation Code with their Quantity								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
Atenolol(mg)	50	50	50	50	50	50	50	50	50
Croscarmellose Sodium (CCS) (mg)	10	20	30	-	-	-	-	-	-
Crospovidone (mg)	-	-	-	10	20	30	-	-	-
Sodium Starch Glycolate (SSG) (mg)	-	-	-	-	-	-	10	20	30
Mannitol (mg)	93	99	93	93	99	93	93	99	93
Microcrystalline Cellulose (MCC) (mg)	80	60	60	80	60	60	80	60	60
Aspartame (mg)	6	6	6	6	6	6	6	6	6
Talc (mg)	5	8	5	5	8	5	5	8	5
Magnesium Stearate (mg)	6	7	6	6	7	6	6	7	6
Total (mg)	250	250	250	250	250	250	250	250	250

Evaluation of Pre-Compression Characteristics of Tablets [21]: -

Prior to the compression, the powder blends are evaluated for their bulk and tapped density. From these values, the compressibility was calculated. While the flow property of the powder blend was accessed from the angle of repose. The evaluation meters were studied before and after the addition of lubricant to check and compare the inherent flow properties of powders.

Bulk density: Apparent bulk density (*b) was determined by pouring the blend into a graduated cylinder. The bulk volume (V*) and weight of the powder (M) were determined. The bulk density was calculated using the formula [14].

$$*b=M/V*$$

Tapped density:

The measuring cylinder containing a known mass of blend was tapped for a fixed time (around 250). The minimum volume (Vt) occupied in the cylinder and the weight (M) of the blend was measured. The tapped density (*t) was calculated using the formula [14]

$$*t=M/Vt$$

Hausner's ratio:

Hausner ratio is an indirect index of ease of powder flow. It is calculated by using the formula

$$Hausner\ ratio = *dt/*$$

Carr's Index (% Compressibility):

The simplest way to measure of free flow of powder is compressibility, an indication of the ease with which a material can be induced to flow is given by the compressibility index (C.I) which is calculated using the formula [21],

$$C.I\ (\%) = \frac{Tapped\ density - Bulk\ density \times 100}{\text{Tapped density}}$$

Angle of repose:

This is the maximum angle possible between the surface pile of powder and the horizontal plane. The frictional forces in the loose powder can be measured by the angle of repose. The tangen an angle of repose is equal to the co-efficient friction (μ) between the particles. Hence the rougher & more irregular the surface of particles the greater will be the angle of repose.

$$\Theta = Tan\text{-}1(h/r)$$

Where, Θ = angle of repose, r=radius of the pile, h=height of the pile,

Table No. 12: Significance of Angle of Repose [6]

Angle of Repose	Type of Flow
25-30	Excellent
31-35	Good
36-40	Fair
41-45	Passable
46-55	Poor
56-65	Very poor
>66	Very, very poor

Evaluation of Post-Compression Characteristics of Tablets:

Tablets were evaluated for their thickness, weight uniformity, hardness friability, disintegration time, and dissolution profiles by using standard procedures.

Thickness: The tablets were evaluated for their coating thickness. The thickness of the core tablet was measured using a vernier caliper (Mitutoyo, Japan) in terms of micrometers. Again, the thickness of coated tablet was measured the difference between the two is calculated Average of three readings was taken and the results were tabulated [14].

Weight uniformity: Ten tablets were taken and weighed individually. The average weight was calculated standard deviation and percent coefficient of variance were computed [14].

Hardness Test: Prepared tablets were evaluated for their hardness by using a Pfizer hardness tester. The hardness was measured in terms of kg/cm2. Triplicate readings were taken and the average was computed. [14]

Friability Test: Roche Friabilator was used for testing the friability of the tablets. Five tablets were weighed accurately and placed in the tumbling chamber and rotated at 25 rpm for a period of 5 min. Tablets were again weighed and the percentage weight loss was determined by using the formula given below. [14]

$$\% \text{ Friability} = \frac{\text{Initial wt. of tablet (W1)} - \text{Final wt. of tablet (W2)}}{\text{Initial wt. of tablets}} \times 100$$

Where, W1 is the initial weight of the tablets W2 is the final weight of the tablet after rotation

Disintegration time: The disintegration test was performed for OFDT tablets in distilled water at 370C by using the USP disintegration apparatus. Triplicate readings were taken and the average was computed.[14]

Drug content uniformity: For determination of drug content, five tablets from each formulation were triturated using mortar and pestle. An accurately weighed powder equivalent to 300 mg of the drug was taken in a 100 ml volumetric flask and diluted with a sufficient amount of 0.1 N HCl up to the mark. Then the sample was sonicated for 1 hr and filtered. An aliquot of the filtrate was diluted suitably and analyzed spectrophotometrically at 220 nm against blank. The test was done in triplicate and average drug content was estimated. [14]

In-vitro dissolution studies [14]: -

Electro lab TDT-06PL USP dissolution test apparatus:

In-vitro dissolution tests of orally disintegrating tablets of Atenolol were performed as mentioned Below: - Dissolution Apparatus: USP Apparatus Type II (Paddle) Dissolution Medium: 0.1N Hydrochloric acid Temperature: - 37±2° C

RPM: 50

Sampling Intervals (min): - 2, 4, 6, 8, 10 min

IV. RESULTS AND DISCUSSION

Pre formulation Study

Solubility Determination

The solubility of the pure drug in 10mg/10ml of solvent was carried out and it reveals that it wasslightly soluble in water (26.5 mg/mL at 37 ºC) Slightly soluble in water**,** soluble in anhydrous ethanol .

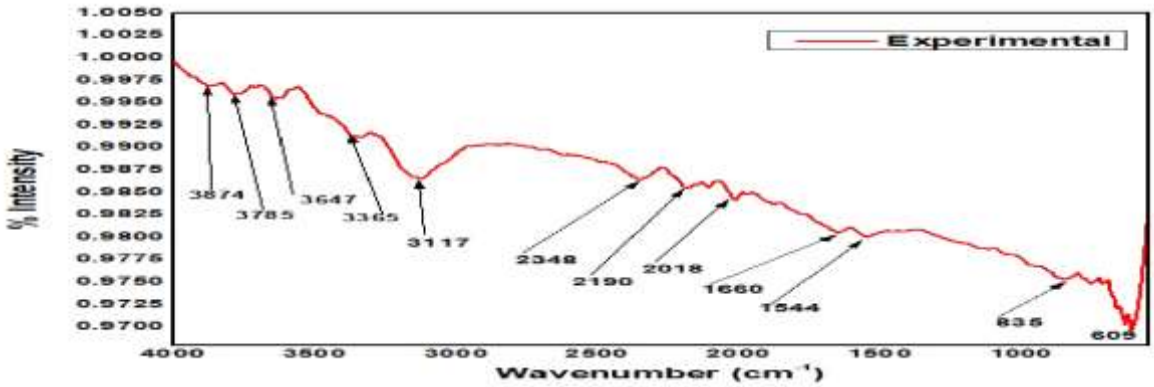
Melting Point Determination

The melting point of Atenolol was also measured in the laboratory and found to be in the range of 146-148°C**.**

Determination of a λ max
λ max of Atenolol in 0.1 HCL was found to be 224nm.

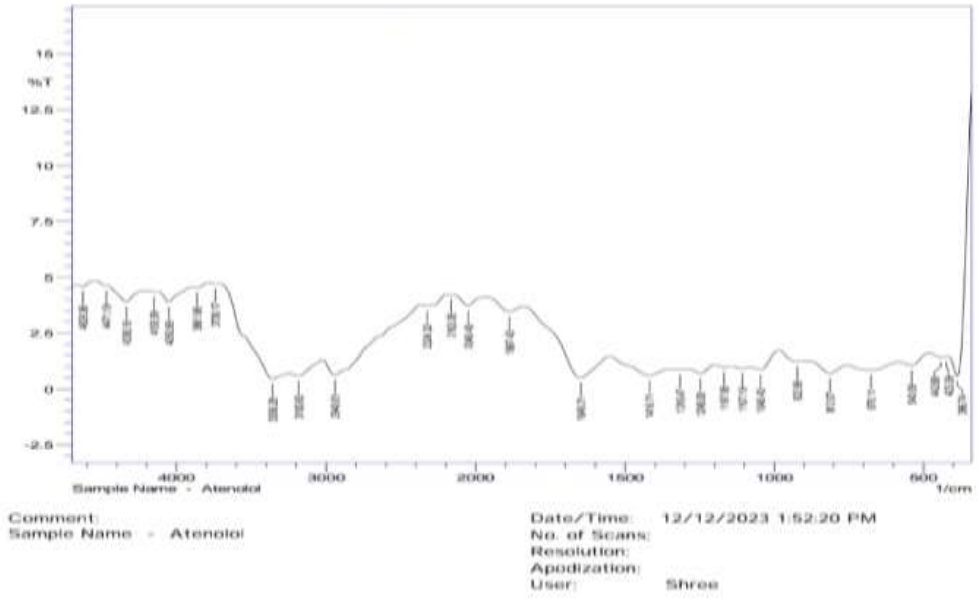
EVALUTION PARAMETER OF ATENOLOL TABLET

Drug polymer compatibility by FTIR studies



Graph No. 1. IR Spectrum of Drug & Excipients

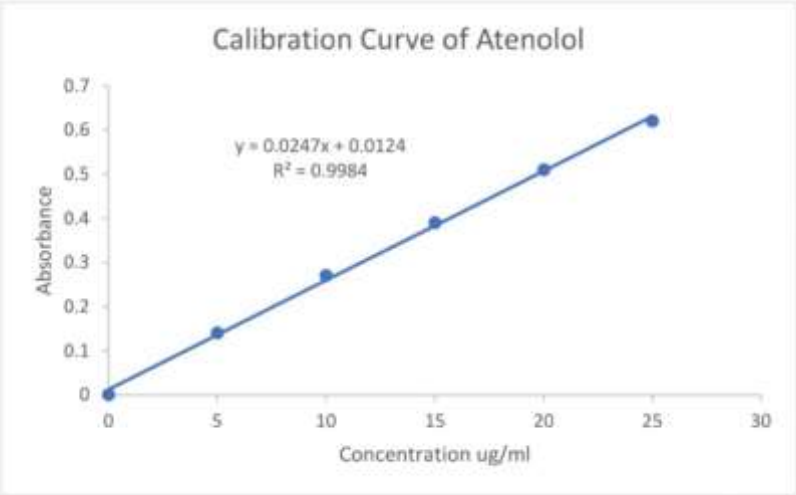
FTIR spectrum of Atenolol: -



Graph No. 2. IR Spectrum of Drug

Standard Calibration Curve for Atenolol in 0.1N HCl

The standard calibration curve of Atenolol was plotted using a UV visible Spectrophotometer at λ max 224 nm by using 0.1 N HCl. A graph of absorbance versus concentration was plotted and was found to be linear, indicating is Compliance with Beer-lambert's law.
Equation, y= 0.0247x+0.0124 R2= 0.9984



Graph No. 2. Calibration curve of atenolol

Evaluation of Mixture Blend of Preliminary Batches

Sr No.	Formulation Code	Bulk density (gm/cm^3)	Tapped density (gm/cm^3)	Angle of Repose	Compressibility index (%)	Hausner 'sratio
1	**F1**	0.382±0.147	0.441±1.632	31.65±0.452	13.3786±0.654	1.15±0.864
2	**F2**	0.345±0.241	0.398±1.538	34.75±0.578	13.3165±0.542	1.13±0.657
3	**F3**	0.391±0.563	0.45±1.357	32.34±1.347	13.1111±0.628	1.15±0.752
4	**F4**	0.392±0.622	0.435±1.863	31.22±1.745	19.8850±1.074	1.16±1.874
5	**F5**	0.335±0.426	0.401±1.752	32.47±1.673	15.9600±0.625	1.18±1.865
6	**F6**	0.360±0.842	0.421±1.572	33.92±0.544	13.5391±1.753	1.12±1.854
7	**F7**	0.337±0.239	0.417±1.347	33.11±0.460	19.1846±0.763	1.15±0.763
8	**F8**	0.373±0.826	0.432±1.896	31.56±0.023	13.6574±0.542	1.13±767
9	**F9**	0.352±0.974	0.409±0.324	34.65±0.103	13.9364±0.653	1.14±0.652

All values are expressed as mean ± standard deviation, n=3

Evaluation of Post Compression Parameters of Preliminary Batches

Parameters	Formulation Code								
	F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
Average Weight (mg)± S.D.	250.02 ± 0.816	249.99 ± 0.923	250.1 ± 1.056	249.95± 1.283	249.98± 1.157	250.05± 0.683	249.76± 0.872	249.25± 0.828	249.1 ± 0.866
Weight Variation test	Passes	Passes	Passes	Passes	Passes	Passes	Passes	Passes	Passes
Thickness (mm) ± S.D.	4.05 ± 0.572	4.1 ± 0.542	4.3± 0.617	4.4± 0.625	4.5± 0.12	4.1± 0.439	4.5± 0.480	4.3± 0.597	4.8± 0.177
Hardness (kg/cm^2) ±S.D.	3.7± 0.42	4.1± 0.29	3.5± 0.36	4.4± 0.31	3.8± 0.17	3.7± 0.35	4.2± 0.25	3.3± 0.23	4.5± 0.32
Friability (%) ± S.D.	0.37±0.15	0.24± 0.92	0.40 ±0.99	0.19 ±0.61	0.34 ±0.96	0.37 ±0.68	0.22 ±0.94	0.45 ±0.85	0.18 ±0.69
Disintegration time (sec) ± S.D.	33.26± 0.03	58.32± 0.12	30.79 ±0.16	65.21 ±0.2	37.19 ±0.12	32.43 ± 0.6	60.86 ±0.22	28.91 ±0.3	71.97 ±0.43
Drug Content (%) ± S.D.	99.43± 0.02	99.66± 0.05	99.31 ±0.03	99.35 ±0.06	99.21 ±0.07	99.22 ±0.03	99.32 ±0.02	99.12 ±0.04	99.77 ±0.02

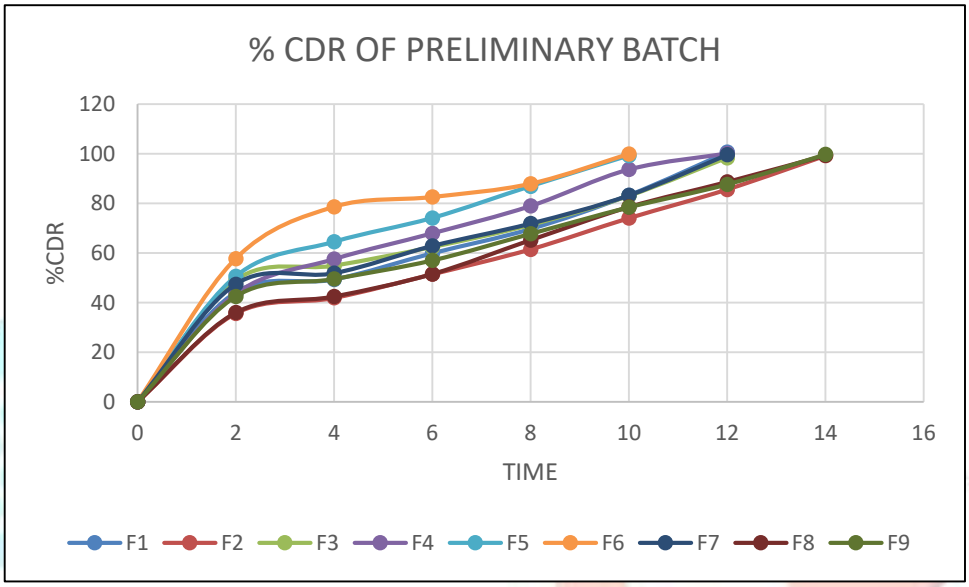
All values are expressed as mean ± standard deviation, n=3

Result for In-Vitro drug release of the OFDT of Preliminary Batches:

Sampling Time (min)	Cumulative % Drug Release in Different Trials								
	F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
0	0	0	0	0	0	0	0	0	0
2	44.14± 1.71	35.66± 1.06	49.10± 0.18	43.60± 1.21	50.59± 1.24	57.72± 1.31	47.43± 0.836	35.98± 0.88	42.50± 1.26
4	49.35± 0.88	41.91± 1.51	54.88± 0.13	57.56± 1.05	64.50± 0.96	78.59± 0.96	51.86± 3.295	42.49± 0.63	49.53± 0.76
6	59.91± 1.32	51.45± 1.48	62.40± 0.72	67.95± 0.90	74.61± 0.61	82.54± 1.35	62.85± 0.552	51.56± 1.33	57.02± 0.68
8	69.69±	61.50±	71.31±	78.96±	86.90±	87.87±	71.86±	65.23±	67.73±

	1.01	0.80	0.63	0.45	0.93	1.23	0.460	0.28	0.73
10	83.27± 0.45	74.06± 0.86	82.99± 0.63	93.68± 1.33	99.24± 0.84	99.90± 0.22	83.20± 0.684	78.56± 0.61	78.43± 0.87
12	100.6± 0.77	85.62± 0.98	98.35± 0.55	100.1± 0.44			99.56± 0.67	88.65± 0.33	87.65± 0.54
14		99.21± 0.66						99.35± 0.76	99.7± 0.56

All values are expressed as mean ± standard deviation, n=3



Graph No. 4. In-vitro Drug Release for Preliminary Batches

Discussion

% Drug Release of Fast dissolving tablet (F1-F9) was found to be range from 98.35±0.61 to 100.6±0.63, 11 was observed that Cumulative Drug release of dissolving tablets depend on the concentration of polymer (Croscarmellose, cross povidone, Sodium starch glycolate). Maximum Cumulative % Drug Release i.e., within 10 min was found 99.90 % for F6 batch, and prolong Cumulative % Drug Release was found 98.28 % within 12 min for F1 batch.

PREFORMULATION STUDY

The solubility of Atenolol reveals that it was freely soluble in methanol and soluble in acetic acid and dimethyl sulfoxide. It is sparingly soluble in 96% ethanol, slightly soluble in water andisopropanol. Melting point of Atenolol was determined by capillary method. The melting point of Atenolol was found to be in the range 146° C to 148° C, which complied with BP standards thus indicating purity of the drug sample. In Pre formulation studies, it was found that, the max of Atenolol by UV spectroscopic method was found at 224 nm in pH6.8 buffer. A standard calibration curve of Atenolol was made in phosphate buffer pH6.8 by taking absorbance V/S concentration between 2-20µg/ml ranges. This complied with BP standards thus indicating purity of obtained drug.

Drug -polymer compatibility by FTIR

FTIR of drug-polymers interaction studies are shown in Graph 1 and Graph 2. It was found that Atenolol was compatible with super disintegrants used in the formulation and there were no extra peaks observed.

Pre-compressionparameters

Pre-compression parameters play an important role in improving the flow properties of pharmaceuticals especially in tablet formulation. These include angle of repose, bulk density, tapped density, carr's index and haunser ratio. Before formulation of tablets the drug and superdisintegrants mixture were evaluated for all the above said parameters and it was found that all the observations were within the prescribed limits of IP.

Angle of repose of all the formulations was found to be raging from 31.22-34.75, bulk density was found to be 0.35-0.39 g/cc, tapped density was in between 0.398- 0.441g/cc, Carr's index was found to be within 13.65-19.88 and haunser ratio was found to be within 1.12-1.18indicating **compressibility of the tablet granules is good as reported in Table.**

PRE COMPRESSION PARAMETER

Average weight and weight variation:

All the formulations (F1 to F9) showed an average tablet weight within the acceptable range of 250 ± 5% mg.The weight variation test for all the batches passed the pharmacopoeial limits, indicating good uniformity in the tablet weights.

Tablet thickness:

The tablet thickness ranged from 4.05 ± 0.572 mm to 4.8 ± 0.177 mm across the different formulations.The slight variation in thickness could be attributed to the differences in the formulation compositions and compression forces used.

Tablet hardness:

The hardness of the tablets varied from 3.3 ± 0.23 kg/cm2 to 4.5 ± 0.32 kg/cm2.The hardness values were within the acceptable range, ensuring adequate mechanical strength for the fast-dissolving tablets.

Tablet friability:The friability values ranged from 0.18 ± 0.69% to 0.45 ± 0.85%, which are well within the pharmacopoeial limit of not more than 1%.The low friability indicates the ability of the tablets to withstand handling and packaging without breaking or chipping.

Disintegration time:

The disintegration time varied from 28.91 ± 0.3 seconds to 71.97 ± 0.43 seconds across the different formulations.The formulations containing higher concentrations of the superdisintegrants (croscarmellose sodium and crospovidone) showed faster disintegration times, meeting the criteria for fast-dissolving tablets.

Drug content:

The drug content uniformity was within the acceptable range of 99.12 ± 0.04% to 99.77 ± 0.02% for all the formulations.This indicates the uniform distribution of the drug in the tablet matrix and successful manufacturing of the fast-dissolving atenolol tablets.

The comprehensive evaluation of the physical, mechanical, and disintegration properties of the atenolol fast-dissolving tablet formulations demonstrated that the optimized formulations, particularly those containing higher levels of croscarmellose sodium and crospovidone, exhibited the desired characteristics for a rapid-dissolving delivery system.

CONCLUSION

The conclusion drawn from the present investigation is given below;

Preformulation studies of Atenolol were performed. From the FTIR the interference was verified and found that Atenolol did not interfere with the polymers used.Nine batches of mouth dissolving tablets of Atenolol were successfully prepared using sodium starch glycolate, crosscarmellose and crospovidone by direct compression method. The tablets were evaluated for parameter like thicknes ,hardness,friability, invitro disintegration time, wetting time, % drug content and in vitro drug release drug.

Based on the results, formulation containing 8% crospovidone (A-5) was identified as ideal and better formulation among all formulations developed for Atenolol tablets.

In vitro release of optimized formulation of Atenolol mouth dissolving tablets of F-5 was found to be 99.6=24% drug release within 10 min. within vitro disintegration time being 37.19sec.

SUMMARY

The present study developed and evaluated fast-dissolving tablets of atenolol, a cardio-selective beta-blocker, to improve patient compliance and therapeutic efficacy. Fast-dissolving atenolol tablets were prepared using direct compression with varying concentrations of superdisintegrants like croscarmellose sodium, crospovidone, and sodium starch glycolate.

The optimized formulation (F5) containing crospovidone (20 mg) showed the fastest disintegration time (44.10 ± 0.31 sec) and maximum cumulative drug release (99.24 ± 0.157% in 10 min).

The developed fast-dissolving atenolol tablets are expected to provide rapid onset of action and improved patient compliance in the management of angina. The comprehensive evaluation showed the optimized formulations containing higher levels of croscarmellose sodium and crospovidone exhibited the desired characteristics for a rapid-dissolving delivery system.

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