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Development Of Fast Dissolving Tablets of Atenolol Using Solid Dispersion Technology

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Abstract

Context: The solid dispersion (SD) dosage plays a vital role in formulating some poorly water-soluble drugs as fast-dissolving dosage forms by modifying the additives and procedures. SD belongs to the combination of solid products composed of two ingredients, usually a hydrophilic carrier & a hydrophobic matrix; where the matrix could be either amorphous or crystalline in form. Amlodipine, a calcium channel blocker widely being employed in hypertension and angina. The fast disintegrating nature of SD amlodipine enhances its rapid action and pharmacodynamics properties. Aim: To develop the fast dissolving solid dispersion formulations of Atenolol employed in the management of Hypertension. Settings and Design: Solvent evaporation process was employed in this

study to prepare the solid dispersion dosage forms of Atenolol using methanol as a solvent.
Methods and Material: The solid dispersion formulations of Atenolol were prepared and evaluated for the XRD, SEM and dissolution. Invitro dissolution analysis was also performed. Results: The drug content uniformity studies, X ray diffraction studies, dissolution studies and scanning electron microscopy was performed to the solid dispersions and indicates the crystalline nature of the preparation. Pre formulation studies have provided an evidence that the powder was suitable for compression process. The atenolol fast dissolving tablets were observed to have preferable drug content. Conclusion: In-vitro dissolution study of atenolol FDS has given an evidence of its high lipophilic and crystalline nature. SD technology and incorporation of superdisintegrants in the tablet formulation containing solid dispersion of drug is a promising methodology to formulate effective FDT of atenolol.

Keywords: Cellular transport, coating, dissolving, fast dissolving tablets

INTRODUCTION:

The oral route is a simpler and easier path to administrate a drug. Nowadays, enhancing the solubility of inadequately soluble drugs for oral delivery is the most significant difficulty in the pharmaceutical industry for the scientist community. The oral drug delivery is a suitable and beneficial route because of its dose accuracy, cost-effectiveness, excellent resistance, higher patient compliance, the flexibility in designing a dosage pattern. The solubility, disintegration, penetration, and bioavailability of the drug are the few processes or mechanisms that lack in the oral delivery of the drugs. If a drug needs to be formulated for the oral route, it must dissolve in both gastric as well as intestinal fluids to reach the systemic circulation by crossing all the barriers. Hence, diffusion rate-limited absorption occurs for the drugs having lower membrane permeability as well as for the drugs having inadequate aqueous solubility. These two main drawbacks in the pharmaceutical industry can be overcome by improving the solubility and the permeability of poorly soluble drugs for attaining higher bioavailability of oral drugs. The solid dispersion dosage plays a vital role in formulating some poorly water-soluble drugs as fast-dissolving dosage forms by modifying the additives and procedures [1]. The inadequate bioavailability is due to the low solublility of the drugs in aqueous medium and lower dissolution rate in GI fluids. This is the major issue in pharmaceutical technology with over 35% of known drugs and over 25% of recent drugs having the same or similar issues [2]. Some techniques for increasing the dissolution and solubility nature of the drug are (i) Decreasing the particle size (ii) using surfactants (iii) prodrug approach (iv) preparing water-soluble complexes (v) Decreasing crystallinity through the formation of solid solutions (vi) salt formation of the drug [3]. However, the efficiency of using a solid dispersion in order to improve dissolution rate has been reliant on optimization of the solvent and carrier. SD belongs to the combination of solid products composed of two ingredients, usually a hydrophilic carrier & a hydrophobic matrix; where the matrix could be either amorphous or crystalline in form. The melting, melting-solvent, and solvent evaporation are some of the different techniques to prepare solid dispersions. In addition with the technique of adding super-disintegrants like croscarmellose sodium, crospovidone, & sodium starch glycolate. These are known to not damage the GI tract as they are used in low quantities in the formulations [4]. Various methods for formulating solid dispersion are available [5]. During the solvent technique process, an organic solvent is used for dissolving the physical mixture of drug and carrier after which it is evaporated continuously to get a transparent, solvent-free layer of solid dispersion. Later, the layer is scrapped and pulverized in a mortar using the pestle to attain a consistency in weight. The principal benefit of this process is thermal decomposition of drugs and carriers is prevented due to the comparatively lower temperatures needed to evaporate the organic solvents [6]. The drug Atenolol comes under the category of beta-blockers. Its mechanism is to block the effect of some natural chemicals like epinephrine in some parts of human body like blood vessels

and heart. Blood pressure and heart rate was lowered because of this action in the body parts. It is very useful in treating unbalanced heart rate rhythm, angina, and heart attack. For treating the high pressure in blood, atenolol is either used alone or in combination with others. It is freely soluble in methyl alcohol, moderately soluble in water, practically insoluble in trichloromethane and moreover soluble in acetic acid [7].

METHODS:

PREPARATION OF SOLID DISPERSIONS

In the solvent evaporation process, methanol is used for the puropose of dissolving drug and hydrophilic polymer. 5 drug, polymer ratios were taken in values of 1:1-5 which were utilized for the formulation of solid dispersion form of atenolol, by taking the subsequent amount of atenolol and polymer in the conical glass and adding methanol for dissolving this mixture. After getting a completely dissolved and clear polymeric extract, the solvent is evaporated by vacuum evaporator at 40ºC and the dispersion is dried and acquired in the desiccator. The dried desiccator mixture is then pulverised and sieved through sieve no.60 [8].

Drug content uniformity

The drug content uniformity was performed for the prepared atenolol solid dispersions. The SDs equivalent to 50mg of atenolol was taken from each batch, and was analyzed for uniformity of drug content. In a 100ml volumetric flask, the precisely measured amount of atenolol solid dispersions was added by dissolving the mixture with a little amount of methanol. The stock solutions which were prepared were also filtered and diluted with a suitable solvent. The Shimadzu UV-visible spectrophotometer is used for measuring the quantity of drug present in the solid dispersion at 225nm [9].

Infrared spectral analysis

The FTIR of the atenolol SD was obtained using Fourier infrared spectrometer. Infrared analysis was performed with potassium bromide disc method, & the value was obtained in the range of 4000 to 400 cm-1. This was conducted to study the compatibility of drug and polymers employed in the preparation.

Powdered X-ray diffraction studies (XRD)

The pure atenolol and solid dispersions were recorded with XpertPro analytical diffractometer by using Cu as a positively charged electrode material (anode). The 2Ɵ angle ranges from 0º – 100º was used for the sample analysis [10].

Scanning electron microscopy (SEM)

For investigation for the surface morphology SEM analysis was performed for atenolol, poloxamer 407, poloxamer 188, and solid dispersions. To mount, a double-faced adhesive tape was used and thin gold palladium layers were used for the purpose of sputtering [11].

Dissolution studies

The dissolving studies were carried out according to the USP-XXIV procedure. It was conducted by using type II apparatus, and the paddles were rotated at 50 rpm having 900ml of 0.1N HCl (pH 1.2) at 37º±0.5ºC. The dissolution study was conducted using solid dispersions equivalent to 50 mg of atenolol. 5 ml of sample were taken at selected period (10, 20, 30, 40, 50, and 60 minutes), and then aliquots that were removed and replaced with fresh medium that had been pre-warmed to 37^0C each time.The measurement of absorbance was performed by UV Spectroscopy at 225nm [12].

PRE-FORMULATION STUDIES

Angle of repose

It was done through fixed funnel technique. The funnel was placed at 2cm height from the burette stand at a fixed position, and then 2 grams of the drug is slowly poured, until it meets that funnel tip. Later, a rough circle is drawn throughout that pile to measure the radius. The following equation (6.1) was used to calculate the angle of repose.

Bulk density

It was ascertain by pouring 2 gm of the drug slowly in a clean, dry and calibrated cylinder. The following equation (6.2) was used to measure the weight and quantity taken up by the sample.

Tapped density

This parameter was evaluated by determining volume through tapping a

calibrated cylinder 2 inches from the base having the powdered drug sample. It is expressed in g/ml [13].

Percentage compressibility

It was used to estimate the flow quality of the drug sample via the bulk and tapped density relation. Also, it is known as the carr's compressibility.

Hausner's ratio

It is a secondary index to calculate the flowability of powder. Low hausner ratio (< 1.25) shows more reliable flow features compared to elevated ratios [14] [> 1.25].

PREPARATION OF FAST DISSOLVING TABLETS

Using various amounts of super-disintegrants, a solid dispersion formulation which demonstrated the maximum drug release was subsequently formulated into tablets. The SDs equivalent to 50 mg of atenolol was used to prepare FDT, and the tablets formulation is given in the Table 1. Mixing of excipients and the drug or its equivalent solid dispersions was performed. Tablet compressions were performed in the (Cadmach 16)station rotary punch tablet machine [15].

Table 1: Atenolol fast dissolving tablets preparation and formulae

Ingredients (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Atenolol SD P407 1:5	300	300	300	300	300	300	300	300	300
Crospovidone	20	25	30	-	-	-	-	-	-
Croscarmellose sodium	-	-	-	20	25	30	-	-	-
Sodium starch glycolate	-	-	-	-	-	-	20	25	30
Magnesium stearate	5	5	5	5	5	5	5	5	5
Talc	5	5	5	5	5	5	5	5	5
Dicalcium phosphate	50	50	50	50	50	50	50	50	50
Microcrystalline Cellulose	65	60	55	65	60	55	65	60	55
Saccharin sodium	5	5	5	5	5	5	5	5	5
Mannitol	50	50	50	50	50	50	50	50	50
Total [mg]	500	500	500	500	500	500	500	500	500

EVALUATION OF ATENOLOL FAST DISSOLVING TABLETS

Uniformity of weight

20 tablets were randomly selected and weighed. Comparison is done individually with avg. weight. The allowed % variation of tablets weighing 500 mg is ± 5 %. The formulated tablets passes the USP test if not more than two tablets are exceed the limit and no tablet differs by more than twice the limit.

Hardness

The randomly selected tablets were placed vertically in the equipment to determine the hardness. Force was applied to break the tablet into 2 parts. The values were noted and expressed in kg /cm^2 [16].

Tablet friability

Friability test is determined by using the Roche friabilator. 20 tablets were selected & then subjected to 100 revolutions. The speed was adjusted to 25 rpm and rotated for 4 min. Prepared formulation were wiped and weighed. Calculation of friability was performed.

Drug content

It is analyzed by selecting 10 tablets and each tablet was made to undergo the determination of the present drug amount. The content of the tablets were in the range of

85-115% of the labelled amount of the drug for all 9 tablets. In case of the 10th tablet it should not contain <75% or >125% of the labelled content. If these conditions were not met the remaining 20 tablets must be analysed individually and all of them should be within the limit [17].

Disintegration test

Based on the capillary action, the disintegration process happens by the water uptake, so the superdisintegrants swells up to break down the tablet. In this study process, 6 tablets were placed individually in each glass tubes and a disc was placed over each of them. 0.1N HCl was used as a media and the temperature maintained at 37ºC ± 2ºC. The complete disintegration time of every tablet was noted down, including the no visible portion of the sample leftover within this disintegration apparatus.

***In-vitro* dissolution study**

USP XXIV dissolution testing apparatus II release rate was caclulated. The invitro dissolution test was performed using 900 ml of 0.1N Hcl at (37º ± 0.5ºC) 50 rpm. At regular intervals, a liquot of dissolution medium was taken and replaced with the same volume of pre-warmed cleaned dissolution medium. The samples were processed, and the drug content released and measured was determined by a Shimadzu-UV spectrophotometer at 225nm. [18].

Results:

Drug content

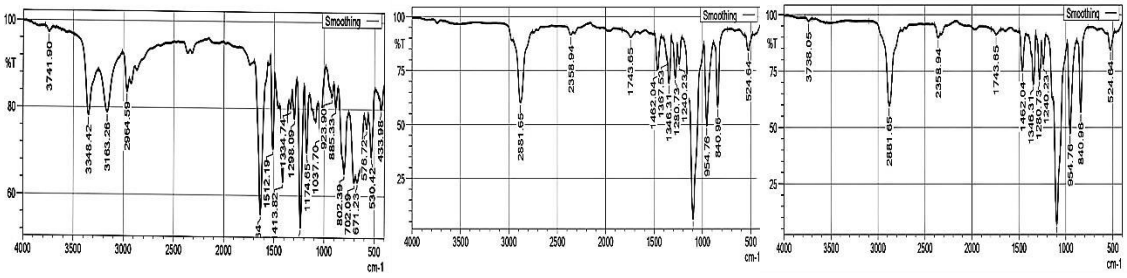
The atenolol SD was investigated by means of UV method at 225 nm and average values was 97.49 ± 2% w/w and results was tabulated in the Table 2 [19].

Table 2: Drug content uniformity of solid dispersions of atenolol

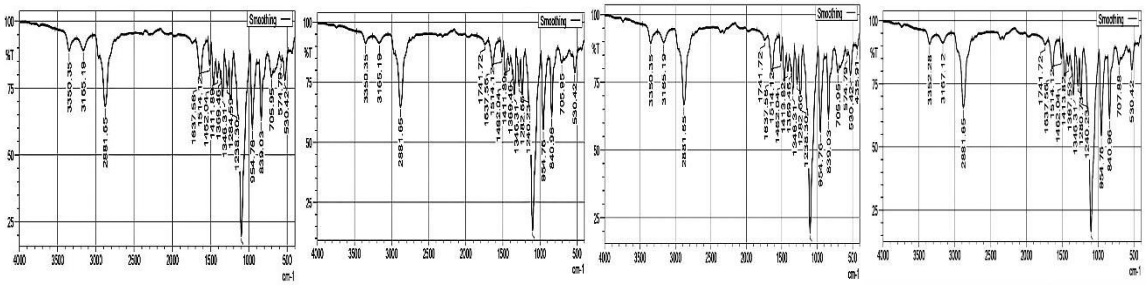
Formulation code	Solid dispersions (Drug: carrier)	% Drug content (n=3)
SD1	(P 407 - 1:1)	95.8 ± 0.42
SD2	(P 407 - 1:2)	97.6 ± 0.46
SD3	(P 407 - 1:3)	98.7 ± 0.55
SD4	(P 407 - 1:4)	99.6 ± 0.19
SD5	(P 407 - 1:5)	96.2 ± 0.49
SD6	(P 188 - 1:1)	98.3 ± 0.28
SD7	(P 188 - 1:2)	97.4 ± 0.65
SD8	(P 188 - 1:3)	95.3 ± 0.36
SD9	(P 188 - 1:4)	99.2 ± 0.71
SD10	(P 188 - 1:5)	96.8 ± 0.39

Infra-red spectral studies

The IR spectral studies of pure atenolol, P 407, P188 and solid dispersions showed characteristic peaks at its respective ranges, and are shown in Figure 1. Because of the N-H stretching, the pure drug spectra reveals a prominent absorption band at 3348.42 cm -1. The band 2964.59 cm-1 may be caused by aromatic and aliphatic C-H bond stretching.The band at 1512.19 cm-1 is for aromatic C=C bond and 1236.37 cm^{-1} is for C = N stretching. The band at 1635.64cm^{-1} is due to C = O & amide group stretching. The spectra of pure P 407 and P 188 matched existing data on the polymer quite well in IR spectral studies.



(a) Pure drug atenolol (b) Poloxamer 407 (c) Poloxamer 188

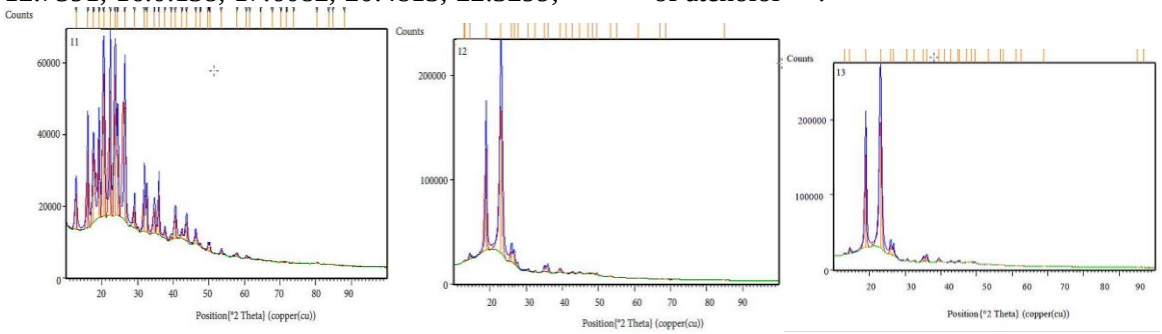


(d) Atenolol P407 SD 1:3 (e) Atenolol P 407 SD 1:5 (f) Atenolol P188 SD 1:3 (g)Atenolol P188 SD 1:5

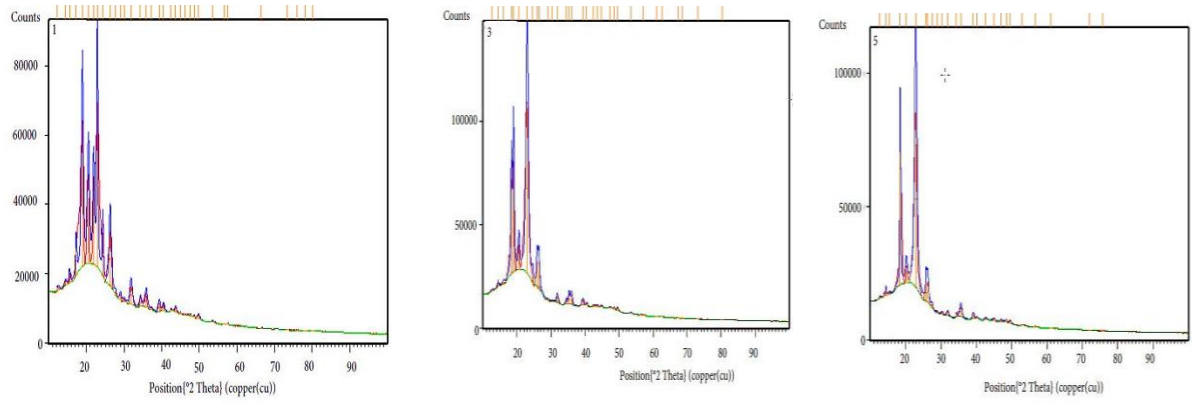
Figure 1: The IR spectral studies of (a) pure atenolol, (b) P 407, P188, (c) Atenolol P407 SD 1:3, (d) Atenolol P 407 SD 1:5, (e) Atenolol P188 SD 1:3, (f) Atenolol P188 SD 1:5

Powdered X-ray diffraction analysis

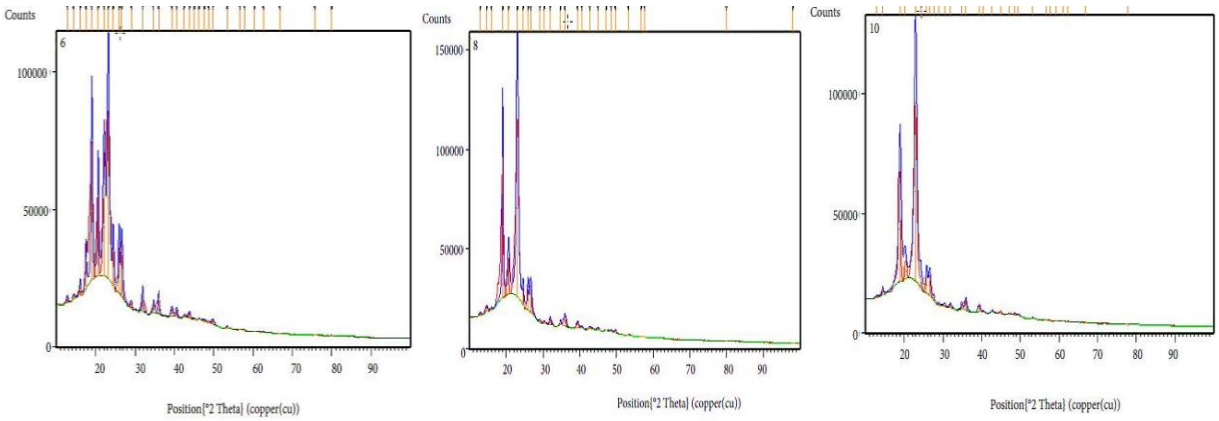
XRD of pure atenolol gave an extremely intense peak due to the high crystallinity. There was found to be sharp diffraction peaks at 2Ɵ degree equal to 12.7591, 16.0.138, 17.6082, 20.4813, 22.3299, and 26.4362 as shown in Figure 2. The results proved the decrease in peak intensity at 2 Ɵ values at 12.7671, 16.0047, 17.4833, 20.5705, 22.1108, and 26.5969 which showed a significant reduction in the crystalline nature of atenolol [20].



(a) Pure drug atenolol (b) Poloxamer 407 (c) Poloxamer 188



(d) Atenolol poloxamer 407 SD 1:1 (e)Atenolol poloxamer 407 SD 1:3 (f)Atenolol poloxamer 407 SD 1:5

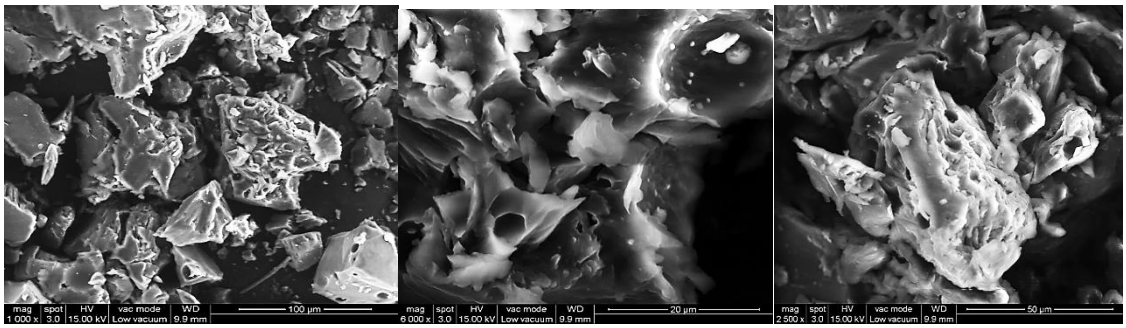


(g) Atenolol poloxamer 188 SD 1:1 (h)Atenolol poloxamer 188 SD 1:3 (i) Atenolol poloxamer 188 SD 1:5

Figure 2: The IR spectral studies of (a) pure atenolol, (b) P 407, (c) P188, (d) Atenolol P407 SD 1:1, (e) Atenolol P407 SD 1:3 (f) Atenolol P 407 SD 1:5, (g) Atenolol P188 SD 1:1, (h) Atenolol P188 SD 1:3 (i) Atenolol P188 SD 1:5

Scanning electron microscopy

SEM analysis of the morphological characteristics of pure atenolol inidicated that the drug was crystalline in character, and the drug particles were found to be irregulaly shaped as shown in Figure 3. The SEM images of solid dispersions of atenolol with P407 & P188 revealed a homogeneous dispersion of particles. This shows that atenolol is dispersed uniformly in the carrier matrices of solid dispersions and were in almost amorphous form [21].



Pure drug atenolol Poloxamer 407 Poloxamer 188

Atenolol P407 SD 1:3 Atenolol P 407 SD 1:5 Atenolol P188 SD 1:3 Atenolol P188 SD 1:5

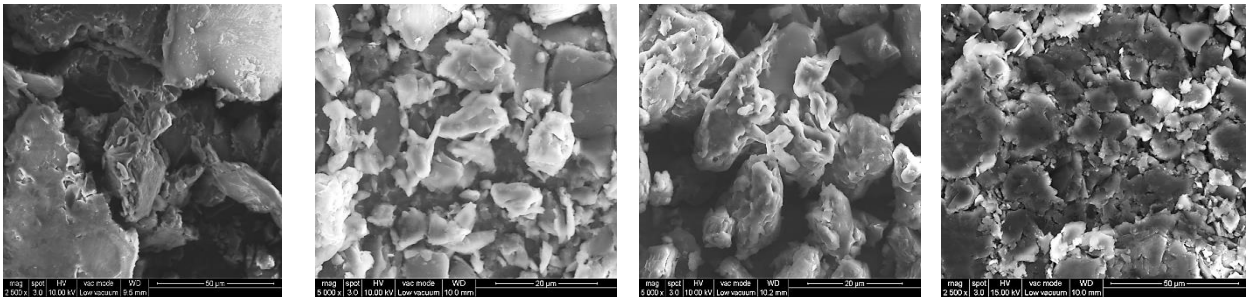


Figure 3: SEM analysis of (a) pure atenolol, (b) P 407, P188, (c) Atenolol P407 SD 1:3, (d) Atenolol P 407 SD 1:5, (e) Atenolol P188 SD 1:3, (f) Atenolol P188 SD 1:5

In-Vitro Dissolution Test of Atenolol Solid Dispersions

Pure atenolol and its solid dispersions were used to perform the dissolution studies. The test was performed up to 60 mins in 0.1N Hcl to clarify the release behaviour. The drug release rate of pure drug showed only 9.8% at 10 min. Also with the case of the drug release rate of atenolol dissolved in 60 mins was found to be 25.2% which shows its lipophilicity and its high crystallinity. This shows a marked enhancement within the release ratio of prepared atenolol SDs with P407. Then, comparing the drug release rate with pure atenolol, the atenolol SD having P407 in the ratio of 1:5 gave highest dissolution rate of 99.2 % at 60 min as shown in Table 3 and Figure 4.

For poloxamer 188 solid dispersions the amount of drug which was released in the 1:1 ratio was 22.7 % at 10 min. This amount of the drug dissolved was increased considerably which is seen in the case of 1:2, 1:3, 1:4, and reached 96.2% of the labeled amount in 1:5 ratio as shown in Table 4 and Figure 5. This result shows the necessity for higher concentration of polymer to convert it into amorphous form and to achieve better dissolution parameters [22-25].

Table 3: In-vitro dissolution data of atenolol P407 SD at different drug:carrier ratios

Time in mins	Percentage drug dissolved from Poloxamer 407 SD					
	Pure atenolol	1:1	1:2	1:3	1:4	1:5
10	9.8	29.2	36.7	43.9	49.8	53.2
20	11.3	37.7	43.6	58.2	69.2	79.5
30	15.4	49.6	55.5	74.3	80.9	86.5
40	19.7	57.9	68.3	82.5	86.7	94.9
50	22.6	61.5	75.9	90.6	92.6	96.7
60	25.2	72.8	86.8	93.9	97.4	99.2

Table:4 In-vitro dissolution data of atenolol SD P188 at different drug:carrier ratios

Time in mins	Percentage drug dissolved from Poloxamer 188 SD					
	Pure atenolol	1:1	1:2	1:3	1:4	1:5
10	9.8	22.7	28.6	36.8	39.5	45.9
20	11.3	35.4	39.3	48.6	55.7	66.8
30	15.4	45.8	53.2	57.2	69.7	75.3
40	19.7	51.6	62.7	66.7	75.8	82.5
50	22.6	62.5	66.9	72.9	80.2	88.3
60	25.2	68.5	75.2	83.5	91.7	96.2

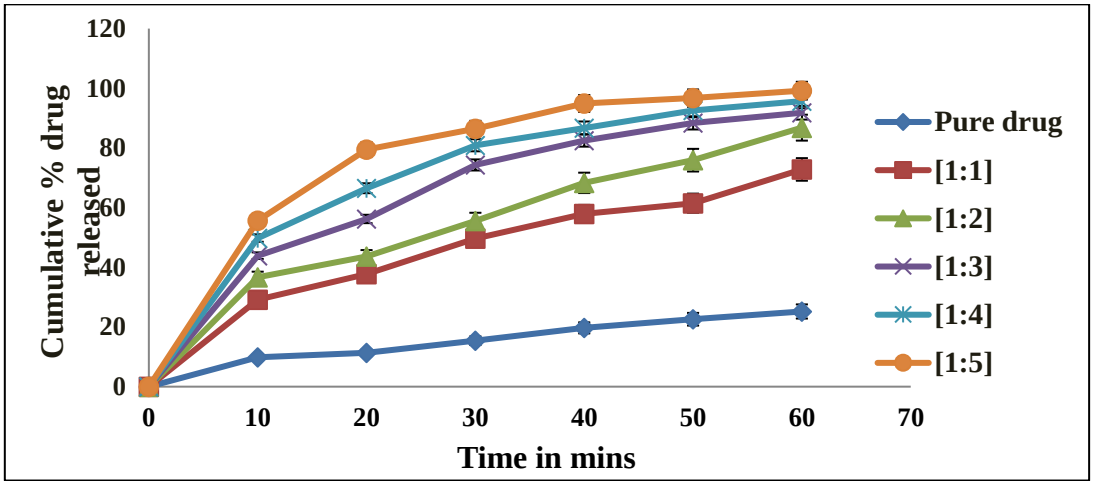


Figure 4:Dissolution profile of atenolol from poloxamer 407 SD at different drug: carrier ratios.

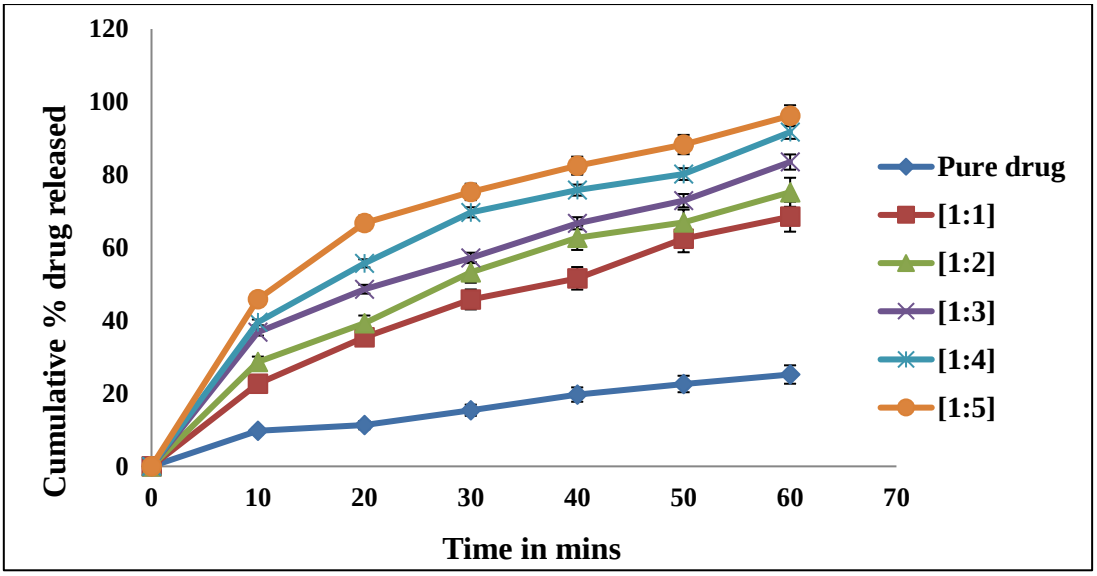


Figure 5: Dissolution profile of atenolol from poloxamer 188 SD at different drug: carrier ratios.

KINETIC TREATMENT OF DISSOLUTION DATA OF ATENOLOL SOLID DISPERSIONS

Table 5: Kinetic studies

Code	Zero-order	First-order	Higuchi	Hixon-crowell	Korsmeyer-peppas	Korsmeyer (Release exponent)	Release kinetics
SD1	0.821	0.9241	0.9601	0.8973	0.985	0.388	Fickian
SD2	0.8577	0.9574	0.9846	0.9499	0.999	0.342	Fickian
SD3	0.7923	0.9842	0.9927	0.9536	0.9857	0.308	Fickian
SD4	0.7452	0.9663	0.9951	0.9536	0.9992	0.276	Fickian
SD5	0.6991	0.9284	0.9704	0.975	0.9965	0.2589	Fickian
SD6	0.8697	0.9531	0.9724	0.9329	0.9892	0.3377	Fickian
SD7	0.8644	0.9603	0.9726	0.9399	0.9688	0.3089	Fickian
SD8	0.8428	0.9427	0.9534	0.9277	0.9626	0.2693	Fickian
SD9	0.8152	0.9613	0.9857	0.9367	0.9971	0.3672	Fickian
SD10	0.7573	0.9353	0.9879	0.9321	0.9709	0.2299	Fickian

EVALUATION OF FAST DISSOLVING TABLETS OF ATENOLOL

Preformulation studies:

The angle of repose shows less than 30 which indicates good flow properties. Bulk density was observed in the range of 0.254 to 0.431 gm/ml, whereas tapped density was observed from 0.358 to 0.533 gm/ml. From bulk & tapped density values, Hausner's ratio& Carr's index was calculated. The % compressibility value was observed between 12.45 to 18.29 %. Hausner's ratio values were

observed to be > 1.25. Therefore, it was shown that the powder blend is suitable for direct compression process [26].

Characterization of tablets:

The results obtained from weight variation test shows that all the tablets are having variation within the limit of ± 5%. The formulated tablets shows that they are uniform in weight.The formulated tablets are having the hardness in the range of 3.1 - 4.3 kg/cm^2. The results showed resistance of prepared tablets to abrasion, capping breakage during storage and transportation.The results of the friability test showed the weight loss in all the prepared tablets were less than 1%. The disintegration test showed that when the proportion of superdisintegrants used in the formulation increased, it decreases the disintegration time of the tablets. This signified that the increasing levels of super disintegrants has a positive impact in the disintegration time of atenolol FDT. The formulated atenolol fast dissolving tablets passes the drug content assay. The results showed that all the tablets batches showed average percentage drug content of more than 98 % [21,27].

In-vitro dissolution study of atenolol FDT:

The dissolution behaviour of various formulations and the control tablets were shown in Table 6 and Figure 6-8. The formulations having the drug release in the following order: F3>F9>F6>F2>F8>F5>F1>F7>F4. A high amount of drug release was seen in crospovidone followed by SSG, and croscarmellose sodium. Highest % release was seen in fast dissolving tablet which contains 6% crospovidone. The control tablets were prepared with crospovidone (6%) with other ingredients using pure atenolol and the dissolution profile is compared with the formulation which contains the solid dispersion of the drug [15,16].

Table 6: *In-vitro* release profile of atenolol fast dissolving tablets

Time in mins	Cumulative percentage drug released									
	Control tablets	F1	F2	F3	F4	F5	F6	F7	F8	F9
5	15.4	45.5	47.1	50.5	43.8	45.8	47.4	44.6	46.5	48.2
10	18.6	51.9	56.8	62.9	49.7	53.5	55.7	51.3	53.9	57.6
20	25.4	61.7	69.1	83.7	62.4	68.6	71.2	65.8	73.9	75.4
30	29.7	66.3	82.6	90.6	69.1	77.3	79.6	72.3	79.9	83.7
40	36.5	74.8	89.7	99.3	77.5	82.9	85.7	79.7	86.5	89.6
50	47.2	78.6	91.9	100	81.7	88.3	92.4	84.6	90.8	94.5
60	51.9	89.7	94.8	100	85.5	91.6	96.8	86.9	93.7	98.4

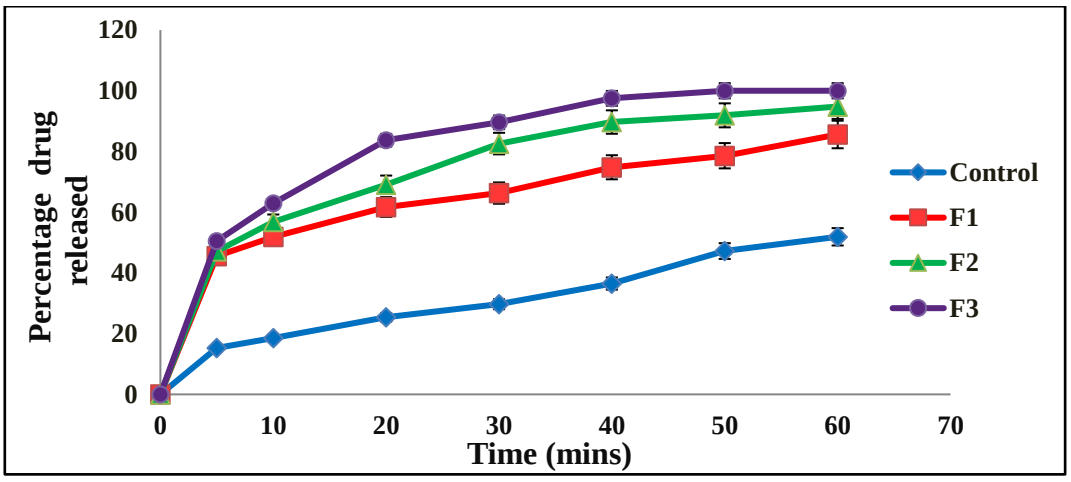


Figure 6: Dissolution profiles of atenolol control tablet and tablets containing SD with crospovidone as superdisintegrant

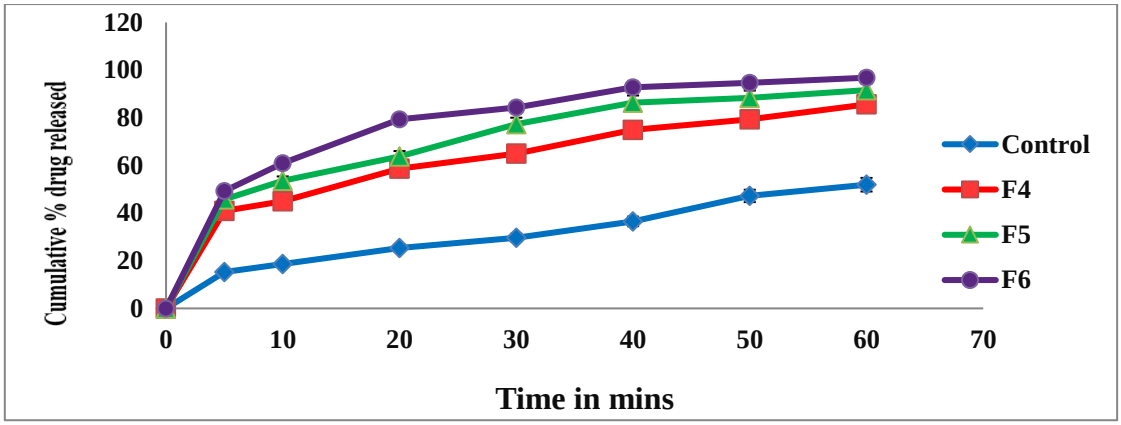


Figure 7: Dissolution profiles of atenolol control tablet and tablets containing SD with Croscarmellose sodium as superdisintegrant

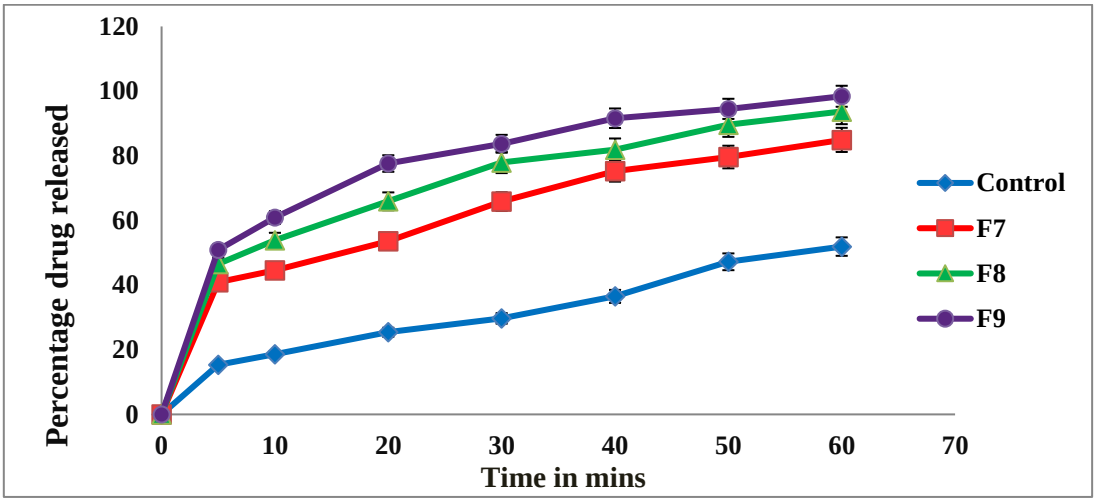


Figure 8: Dissolution profiles of atenolol control tablet and tablets containing SD with Sodium starch glycolate as superdisintegrant

COMPARISON OF DISSOLUTION DATA OF ATENOLOL FDT (F3) WITH MARKETED FORMULATION

The evaluation of dissolution data of atenolol FDT (F3) using marketed tablet clearly showed the rapid and fast release of drug from formulated tablet. The tablet formulation F3 gave 50.5 % of drug releases at 5 min and the drug release reached 100 % at 50 min which is much greater than the marketed atenolol tablet (ATEN^{TM}-50) zydus cadila as shown in Table 7 and Figure 9.

Table 7: Comparison of dissolution data of atenolol fast dissolving tablets (F3) with marketed formulation

S.No	Cumulative percentage drug released		
	Time in min	F3	Marketed formulation
1	5	50.5	32.7
2	10	62.9	39.4
3	20	83.7	46.8
4	30	90.6	57.3
5	40	99.3	63.9
6	50	100	71.6
7	60	100	78.5

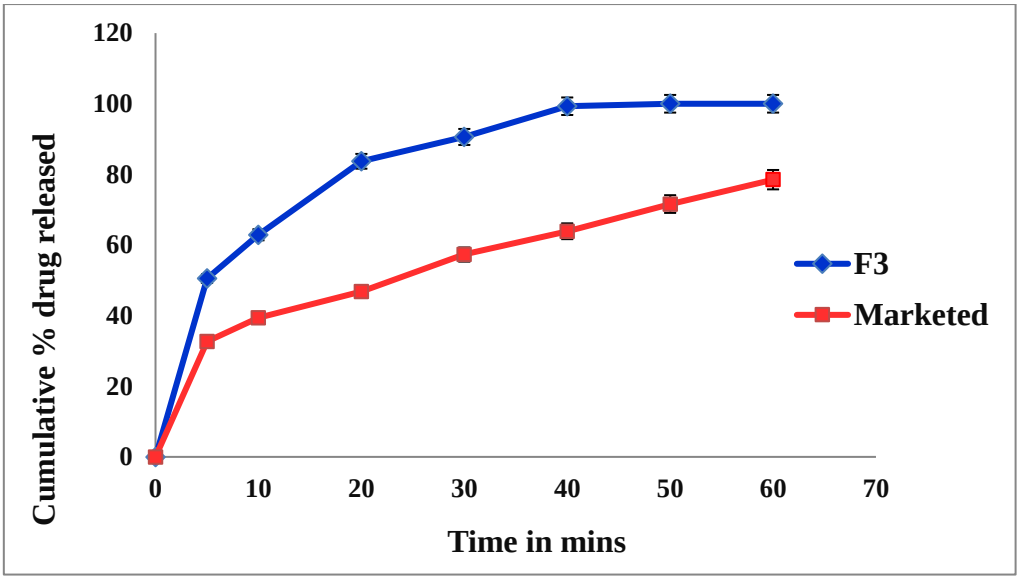


Figure 9: Comparison of dissolution profile of atenolol FDT (F3) with marketed formulation

KINETIC TREATMENT OF DISSOLUTION DATA OF SOLID DISPERSIONS OF ATENOLOL FAST DISSOLVING TABLETS

Table 8: Kinetic studies

Code	Zero-order	First-order	Higuchi	Hixon-crowell
Control	0.9522	0.9711	0.9527	0.968
Marketed	0.8595	0.9667	0.9908	0.9441
F1	0.7575	0.923	0.9808	0.8982
F2	0.7509	0.9799	0.9746	0.9307
F3	0.7015	0.9057	0.9229	0.9696
F4	0.7593	0.9512	0.9948	0.902
F5	0.753	0.9718	0.9872	0.9208
F6	0.7653	0.972	0.9931	0.9526
F7	0.7476	0.9506	0.9878	0.8979
F8	0.7428	0.9754	0.9669	0.9211
F9	0.7479	0.9686	0.9783	0.957

Table 9: Coefficient of determination (r^2)

Formulation code	Korsmeyer-peppas	Korsmeyer (Release exponent)	Release kinetics
Control	0.9575	0.4925	Non-Fickian
Marketed	0.9798	0.3512	Fickian
F1	0.9714	0.2587	Fickian

F2	0.9905	0.2957	Fickian
F3	0.9672	0.2904	Fickian
F4	0.9923	0.2804	Fickian
F5	0.9953	0.2898	Fickian
F6	0.997	0.294	Fickian
F7	0.9937	0.2818	Fickian
F8	0.9832	0.2967	Fickian
F9	0.9928	0.2956	Fickian

DISCUSSION:

The studies were undertaken on the preparation and evaluation of solid dispersions of atenolol with a view to develop FDT of atenolol. The SD was prepared by solvent evaporation technique using poloxamer 407 and poloxamer 188 in various ratios like 1:1, 1:2, 1:3, 1:4 and 1:5.

From the infra-red spectral analysis, there was found to have no significant interaction in-between drug & the carriers utilized in the development of SD. The SD of all preparations was found to be uniform in drug content. The XRD studies revealed that the crystalline nature of pure atenolol was reduced in the solid dispersions. This might be the reason for improved dissolution and also indicated amorphous character of the atenolol in solid dispersions. Scanning electron microscopy showed that the drug is uniformly dispersed in solid dispersions.

Results of dissolution studies revealed a quick & rapid dissolution of atenolol SD when related to pure drug. Amongst the carriers used, poloxamer 407 in the ratio of 1:5 in solid dispersions gave the fastest dissolution rate.

The solid dispersions atenolol with poloxamer 407 in the ratio of 1:5 were formulated into fast dissolving tablets utilizing various ratios of SSG, croscarmellose sodium, & crospovidone as superdisintegrants.

Friability test in all the formulation was found to be less than 1% which indicates the resistance to abrasion. Hardness of the prepared formulation was from 3.1 - 4.3 kg/ cm^2. It was observed to be uniform in weight, and variation in weight was within the limit of ±5%. The drug content also observed to be uniform. I*n-vitro* dissolution of the formulation was found to increase with increase in super disintegrant level.

Comparing the *in vitro* dissolution profile of atenolol fast dissolving tablets (F3) with control tablets also with marketed formulation (ATEN^{TM}-50) showed rapid and enhanced drug release compared with marketed tablet. These low values of the release exponent (>0.45) indicated that the drug release of all formulations could be described as a Fickian Diffusion mechanism.

The formulation of FDT using solid dispersion method is a unique technique by which the dissolution rate of atenolol can be enhanced which is the most challenging aspect of drug delivery. Hence, it has been concluded that the combination of SD technology and incorporation of super disintegrants in the tablet formulation containing solid dispersion of drug is a promising methodology to formulate effective FDT of atenolol.

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Conflict of interest:
The authors report that there is no conflict of interest

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