Research Article

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DEVELOPMENT AND EVALUATION OF FAST DISSOLVING TABLETS OF DILTIAZEM HYDROCHLORIDE

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Received on: 25/03/15 Revised on: 20/04/15 Accepted on: 30/04/15

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DOI: 10.7897/2277-4343.06494

ABSTRACT

The aim of present work was to develop fast dissolving tablets of Diltiazem hydrochloride by direct compression method using different superdisintegrant such as crospovidone (CP), croscarmellose sodium (CCS) and sodium starch glycolate (SSG). The prepared tablets were evaluated for pre-compression parameters such as angle of repose, bulk density, compressibility index, Hausner's ratio and post-compression parameters such as thickness, hardness, friability, drug content, weight variation, wetting time, water absorption ratio, in-vitro disintegration time, *In-vitro* dissolution studies and stability studies. All the parameters showed good results. IR and DSC study showed that drug and excipients were compatible with each other. The study reveals that formulations prepared by direct compression F3 exhibits highest dissolution using crospovidone at concentration of 4.5 % & showed faster drug release 91.72 % over the period of 15 min while disintegration time of the tablet was showed 37 sec comparison to other formulations of Diltiazem hydrochloride.

Keywords: Fast dissolving tablets, Diltiazem hydrochloride, direct compression, crospovidone.

INTRODUCTION

United States Food and Drug Administration (US-FDA) defined fast dissolving tablet (FDT) as "a solid dosage form containing medicinal substance or active ingredient which disintegrate rapidly usually within a matter of seconds when placed upon the tongue." Fast dissolving tablets are also known as mouth-dissolving tablets, melt-in mouth tablets, orodispersible tablets, rapimelts, porous tablets, quick dissolving tablet. Fast dissolving tablets dissolve or disintegrate in the oral cavity without the need of water. Most fast dissolving tablets must include substances to mask the bitter taste of the active ingredient. This masked active ingredient is then swallowed by the patient's saliva along with the soluble and insoluble excipients.[1,2] It has been concluded that faster the dissolution, faster the absorption (only the unionized form of drug) and onset of action. Some drugs are absorbed from the oral cavity, pharynx and esophagus as the saliva passes down into the stomach. Thus the bioavailability of drug is significantly more than those observed from conventional tablets dosage form. The time for disintegration of fast dissolving tablets is generally considered to be less than one minute. [3]

The fast dissolving solid dosage form turns into a soft paste or liquid form for easy swallowing and thus it is free of risk of choking. In recent years, a variety of improved methods for delivering drugs have been developed with the aim of improving bioavailability, convenience and patient compliance. Some tablets are designed to dissolve in saliva within a few seconds, and so called true fast-dissolving tablets.[4]

Objectives

To develope and evaluate fast dissolving tablets of Diltiazem hydrochloride using different superdisintegrants.
To evaluate for the pre-compression parameters of powder mixture like bulk density, flow property, angle of repose, compressibility index and hausner's ratio.
To investigate the possibility of interaction between the polymers and copolymers and also between polymers and drugs by FTIR and DSC.
To evaluate the post-compression parameters of the tablet like hardness, friability, drug content, weight variation, wetting time, water absorption ratio, disintegration time.
To carry out *In vitro* dissolution studies of the tablet formulations.

MATERIALS AND METHODS

Diltiazem hydrochloride was obtained as a gift sample from Balaji Drugs, Gujarat, crospovidone, crosscarmellose sodium, sodium starch glycolate, microcrystalline cellulose, mannitol, orange flavour, talc, magnesium stearate were purchased from S.D. Fine Chemicals, Mumbai.

Fast dissolving tablets of Diltiazem hydrochloride were prepared for F1 to F9 batches by using different concentrations of superdisintegrants mentioned in Table 1 keeping total weight (200 mg) of the tablet constant in all the formulations.Fast dissolving tablets of Diltiazem hydrochloride were prepared by direct compression

method. The drug and excipients were passed through sieve no (#60) to ensure better mixing. Microcrystalline cellulose was used as a direct compressible material. Superdisintegrants like sodium starch glycolate, croscarmellose sodium and crospovidone were used in different concentration. All the ingredients were mixed in mortar and pestle then magnesium stearate and talc were added. The formulations were compressed with a tablet compression machine using 8 mm diameter round concave punch. (Karnavati, mini press-I). Before tablet preparation, the mixture blend subjected for compatibility studies IR, DSC and precompression parameters like angle of repose, bulk density, tapped density, percent compressibility & Hausner's ratio.

In this formulation from batch no. F1 to F3, F4 to F6 & F7 to F9 concentration of microcrystalline cellulose decrease from 71 mg to 65 mg and concentration of superdisintegrants (crospovidone, crosscarmellose sodium & sodium starch glycolate) increase from 3 mg to 9 mg (1.5 to 4.5 %).

Analytical Methods

Preparation of phosphate buffer (pH 6.8)

Dissolve 28.80 gm of disodium hydrogen phosphate and 11.45 gm of potassium dihydrogen phosphate in sufficient water to produce 1000 ml. [5, 6]

Preparation of Diltiazem hydrochloride standard stock solution (100µg/ml) in phosphate buffer (pH 6.8) solution

A standard stock solution of Diltiazem hydrochloride was prepared by dissolving accurately weighed 100 mg of Diltiazem hydrochloride in phosphate buffer (pH 6.8) solution in a 100 ml volumetric flask and the volume was made up to 100 ml by using phosphate buffer (pH 6.8) solution to obtain a primary stock solution of 1000 µg/ml. 1ml of primary stock solution was further diluted to 100 ml phosphate buffer (pH 6.8) to obtain a secondary stock solution of 100µg/ml. [7]

Calibration curve of Diltiazem hydrochloride in phosphate buffer pH 6.8 solution:-

An accurately weighed 100 mg of Diltiazem hydrochloride was dissolved in 100 ml of phosphate buffer (pH 6.8) to get a concentration of 1000 µg/ml. 1ml from above solution was further diluted to 100 ml phosphate buffer (pH 6.8) to obtain a stock solution of 100µg/ml. From this stock solution, aliquots with suitable dilutions were made in order to get concentration in between the Beer's range of 2-14 µg/ml. The dilutions of 2µg/ml, 4µg/ml, 6µg/ml, 8µg/ml, and 10µg/ml were prepared. The absorbance was measured at 237 nm using UV spectrophotometer (Model: Shimadzu 1800, Japan). The standard curve was obtained by plotting absorbance v/s concentration in µg /ml. [8]

Preformulation Studies

The following Preformulation studies were performed for Diltiazem hydrochloride and polymers.

Determination of melting point

Melting point was determined by taking small amount of Diltiazem hydrochloride in a capillary tube closed at one end. The capillary tube was placed in an electrically operated melting point apparatus and the temperature at which the drug melts was recorded. This was repeated three times and average value was calculated. [9]

Drug-excipients compatibility studies

Excipients were integral components of almost all pharmaceutical dosage forms. The successful formulation of a stable and effective solid dosage forms depends on the selection of excipients, which are added to facilitate administration of the drug and protect it from degradation. [10]

Interference of polymers in UV determination of the drug

It is necessary to verify the interference of polymers in UV determination of the drug during the analysis. Keeping in view of the concentration of polymer, an empirical concentration was fixed for the study of interference of polymers. Solutions of polymers were prepared in phosphate buffer (pH 6.8) solution and were scanned in UV spectrophotometer between 200-400 nm using phosphate buffer (pH 6.8) as blank solution. [11]

FT-IR Studies

FT-IR spectroscopy (Model: Synthesis Monitoring System) was employed to ascertain the compatibility between Diltiazem hydrochloride and selected polymers. The pure drug, drug-polymers combinations and formulations were subjected to FT-IR studies. Potassium bromide, pure drug and the polymers were heated to 105^0C for one hour to remove the moisture content if present in a hot air oven. Then in presence of IR lamp, potassium bromide was mixed with drug and or polymer in 9:1 ratio. Grinding in smooth mortar can effect mixing. The mixtures were then placed in the sample holder of the instrument and the spectra were taken. The spectra were run from 4000 cm^{-1} to 1000 cm^{-1} wave number. FT-IR spectrum of Diltiazem hydrochloride was compared with FT-IR spectrum of Diltiazem hydrochloride with polymer. The pure drug and the drug with excipients were scanned separately.

Differential scanning calorimetry (DSC) studies

The DSC analysis (Model: Diamond DSC) was carried out to identify the compatibility between the drug and other excipients. All the samples were run at a scanning rate of 10 °C/min from 50-350 °C.

Solubility studies

Solubility of Diltiazem hydrochloride was determined; it is freely soluble in water, formic acid, chloroform, methanol, insoluble in ether, sparingly soluble in absolute alcohol. Solubility studies were performed by taking 1gm Diltiazem hydrochloride in 10 ml solvent. [12]

Evaluation of tablets
Precompression parameters
Micromeritic properties

Angle of repose ( )

Angle of repose is defined as the maximum angle possible between the surface of a pile of the powder and horizontal plane. The frictional force in a loose powder or granules can be measured by angle of repose[13].

$$\tan \theta = h / r$$
$$\theta = \tan^{-1} (h/r)$$

Where, θ is the angle of repose, h is height of the powder cone, r is radius of the powder cone

Different ranges of flow ability in terms of angle of repose are given in Table 2.

Bulk density

The bulk density of a powder depends primarily on particle size distribution, particle shape, and the tendency of the particles to adhere to one another. [14]

Both loose bulk density (LBD) and tapped bulk density (TBD) were determined. Accurately weighed sample taken in a 25 ml measuring cylinder and measured volume of packing and tapped 100 times on a plane hard wooden surface and tapped volume of packing recorded and LBD and TBD were calculated using following formula;

$$\text{LBD} = \frac{\text{Weight of the powder}}{\text{Volume of the packing}}$$

$$\text{TBD} = \frac{\text{Weight of the powder}}{\text{Tapped volume of packing}}$$

Percent compressibility

Percent compressibility of powder mixture was determined by Carr's compressibility index calculated by following formula. [15]

$$\text{Carr's index} = \frac{\text{Tapped density} - \text{Bulk density}}{\text{Tapped density}} \times 100$$

Hausner's ratio

Hausner's ratio is an indirect index of ease of power flow. It is calculated by the following formula. [16]

$$\text{Hausner's ratio} = \frac{\text{Tapped Density}}{\text{Bulk Density}}$$

Postcompression Parameters
Size and shape of tablets

The size and shape of the tablet can be dimensionally described, monitored and controlled.

Thickness

The thickness of the tablet was measured by using Screw Gauge and expressed in mm. The limit specified was average thickness ± 5% deviation.

Hardness test

The hardness of the tablets was determined using Precision dial type hardness tester. It is expressed in Kg/cm^2. Three tablets were randomly picked from each formulation and the mean and standard deviation values were calculated. [17, 18]

Friability test

The friability of tablets was determined by using Friabilator. It is expressed in percentage (%). 10 tablets were initially weighed ($W_{initial}$) and transferred into friabilator. The friabilator was operated at 25 rpm for 4 minutes or run up to 100 revolutions. The tablets were weighed again (W_{final}). The percentage friability was then calculated by,

$$F = \frac{W_{initial} - W_{final}}{W_{initial}} x100$$

% Friability of tablets less than 1% is considered acceptable. [19, 20]

Weight variation test

The 10 tablets were selected randomly from each formulation and weighed individually to check for weight variation. The in Table 3 percentage deviation in weight variation is allowed.

In all the formulations the tablet weight was more than130 mg and less than 324 mg, hence 7.5% maximum differences allow.

Drug content uniformity

Five tablets were weighed and crushed with pestle in a small glass mortar. The fine powder was weighed to get 200 mg (equivalent to 60 mg of Diltiazem Hcl), and transferred to 250 ml conical flask containing 100 ml of Phosphate buffer pH 6.8 stirred for 45 min in ultra sonicator then solution was filtered and the filtrate obtained was analyzed by UV spectrophotometrically at 237 nm & drug content was determined. [21]

Wetting time

A piece of tissue paper (12cm x 10.75cm) folded twice was placed in a Petri dish (6.5 cm internal diameter) containing 6 ml of phosphate buffer pH 6.8. A tablet was carefully placed on the surface of the tissue paper and allowed to wet completely.

Water absorption ratio

A piece of tissue paper folded twice was placed in a small Petri dish (10 cm diameter) containing 6 ml of phosphate buffer ph 6.8. A tablet was put on the tissue paper and allowed to wet completely. The wetted tablet was then reweighed. Water absorption ratio, R was determined using following equation.[22]

$$R = 100 \frac{(W_a - W_b)}{W_b}$$

Where, W_b – weight of tablet before absorption, W_a – weight of tablet after absorption

Three tablets from each formulation were used and standard deviation was also determined.

***In-vitro* disintegration time**

The *in-vitro* disintegration time of a tablet was determined using disintegration test apparatus as per I.P. specifications. Place one tablet in each of the 6 tubes of the basket. Add a disc to each tube and run the apparatus using phosphate buffer (pH 6.8) maintained at 37 ±2 C as the immersion liquid. The assembly should be raised and lowered between 30 cycles per minute in the pH 6.8 maintained at 37 ±2 C. The time in seconds taken for complete disintegration of the tablet with no palpable mass remaining in the apparatus was measured and recorded.

***In-vitro* dissolution studies**

In-vitro drug release of tablets was studied by using USP type-II apparatus (USP XXIII Dissolution Test Apparatus) at 50 rpm using 900 ml of phosphate buffer pH 6.8 as dissolution medium. The temperature of the dissolution medium was maintained at 37 0.5°C; 5 ml of the sample from dissolution medium was withdrawn at every 3 min interval and filtered through whatman filter paper. The absorbance of sample was measured by UV spectrophotometric method at 237 nm and Cumulative percent drug release was calculated by using an equation obtained from a standard calibration curve. [23]

Stability studies

Stability studies were carried out on optimized tablet formulation. Formulations were stored at 40^0C ± 2^0C / 75 ± 5 % RH for 30 days. After 30 days samples were withdrawn and tested with regards to the parameters i.e. thickness, hardness, drug content and drug release study.

RESULTS & DISCUSSION

Preformulation Studies

Melting point

The melting point of Diltiazem hydrochloride was determined by capillary tube method and it was found to be 210-212^{0}C which is same as that of literature value.

Drug-excipients compatibility studies

FTIR studies

To study the compatibility of the drug with various polymers, FT-IR spectroscopy (Model: Synthesis Monitoring System) of drug and formulation components were carried out.

Differential scanning calorimetry

DSC analysis (Model: Diamond DSC) sharp melting transition of Diltiazem hydrochloride pure drug was observed at 216.20°C. In optimized batch F3 melting endotherm at 214.08°C was observed. This confirmed that the presence of other excipients did not affect the drug nature and it was well maintained in the selected formulation.

Formulation Design

Fast dissolving tablets of Diltiazem hydrochloride were prepared to enhance overall bioavailability by using direct compression method. Total nine formulations were prepared in which the concentrations of superdisintegrants is different to evaluate the effect on the disintegration time of Diltiazem hydrochloride fast dissolving tablets.

Evaluation of tablets

Precompression evaluation parameters

Angle of repose (θ): The values were found to be in the range of 22.48^0 to 28.71^0. All formulations showed the angle of repose within 29^0. It indicates that all formulations showed good flow properties.

Bulk density: - Both loose bulk density LBD and tapped bulk density results are shown in table 6.3. The loose bulk density and tapped bulk density for all the formulations varied from 0.39 gm/cm^3 to 0.45 gm/cm^3 and 0.49 gm/cm^3 to 0.54 gm/cm^3 respectively.

Percentage compressibility:- The percent compressibility of powder mix was determined by Carr's compressibility index. All formulations are showing good compressibility.

Hausner's ratio: - Hausner's ratio of the powder was determined from the loose bulk density and tapped bulk density. Hausner's ratio of all the formulations lies within the acceptable range. The Hausner's ratio of all the formulations is in the range of 1.15 to 1.31.

Post-compression evaluation parameters

Size, shape and color of tablets: - Randomly picked tablets from each formulation batch examined under lense for shape and in presence of light for color. The tablet shows flat, ovate shape and white in color. All ingredients used were white in color. There was no change in color and odor of the tablets in all the formulations. It indicates that all the excipients used were compatible with the drug and did not cause any chemical reaction that affects the properties of formulation.

Thickness:- The thickness of the tablets was measured by using Screw Gauge by taking the tablets randomly. The values are almost uniform in all formulations. Thickness was found in the range from 4.00±0.02 mm to 4.05±0.05 mm respectively.

Hardness test:- Hardness test was performed by Monsanto hardness tester or Precision dial type hardness tester. Hardness was maintained to be within 3.01±0.48 kg/cm^2 to 3.73±0.57 kg/cm^2, as these tablets are mouth dissolving.

Friability:- The result was found well within the approved range (<1%) in all the formulation. Friability was in between 0.57% to 0.74%. Results revealed that the tablets possess good mechanical strength.

Weight variation test:- All the tablets passed weight variation test as the % variation was within the pharmacopoeia limit of ±7.5 %. The weight of all the tablets was found to be uniform.

Drug content uniformity:- The content uniformity was performed for all nine formulations. Five trials from each formulation were analyzed spectrophotometrically. The mean value and standard deviation of all the formulations were calculated. The drug content of the tablets was found between 97.41 to 92.57 % of Diltiazem hydrochloride.

Wetting time:- Wetting is closely related to inner structure of tablets and the hydrophilicity of excipients. The wetting time of the tablets was found between 42±1.45 to 59±1.53sec. The wetting time in all the formulation was very fast.

Water absorption ratio:- The values of formulations found in the range of 76.21 to 95.48. The water absorption increased due to high swelling property.

***In-vitro* disintegration time:-** The internal structure of tablets that is pore size distribution, water penetration into tablets and swelling of disintegration substance are suggested to be the mechanism of disintegration. All the formulations show disintegration time less than 55 seconds. Disintegration time was observed in order of Crospovidone < Croscarmellose sodium < Sodium starch glycolate.

***In-vitro* dissolution studies:-** All the nine formulations were subjected for the *in vitro* dissolution studies using tablet dissolution tester (USP) TDT-08L, Electro lab. The samples were withdrawn at different time intervals, filter, diluted and analyzed at 237 nm. Cumulative drug release (mg) and Cumulative % drug release were calculated on the basis of mean amount of Diltiazem hydrochloride present in the respective tablet. The rapid dissolution was observed in formulations F1, F2, F3 releases 84.46%, 86. %, 91.72% of drug respectively, at the end of 15 minutes. Formulations F4, F5 and F6 which shows drug release 83.27%, 83.80%, 88.17% respectively at the end of 15 min. Formulations F7, F8, F9 releases 82.25%, 83.13%, 88.51% respectively at the end of 15 minutes. This rapid dissolution might be due to fast breakdown of particles and rapid absorption of drug. The drug release was completely achieved in a shorter duration of time. In all the formulations the drug release within 15 minutes. High dissolution may occur due to faster breakdown.

Stability studies:-The results of stability studies were given in table 6.8. After analysis it was found that there were no substantial changes in all parameter of optimized batch (F3). The results revealed that product is sufficiently stable for the period of 30 days at 40^{0}C ± 2^{0}C / 75 ± 5 % RH.

CONCLUSION

Preformulation studies of Diltiazem hydrochloride were performed; the FT-IR and DSC analysis revealed that the superdisintegrants and excipients used were compatible with Diltiazem hydrochloride. Fast dissolving tablets of Diltiazem hydrochloride can be prepared by direct compression method using superdisintegrants like crospovidone, croscarmellose sodium, sodium starch glycolate. Amongst all the formulations, containing crospovidone as superdisintgrants is fulfilling all the parameters satisfactorily. It has shown excellent in-vitro disintegration, in-vitro dissolution compared to other superdisintegrants. Apart from all the formulations of F3 formulation showed maximum drug release (91.72 %) at the end of 15 min.

From the data it can be concluded that there were no appreciable change in physical characteristic were observed in optimized batch (F3) after stability testing. Therefore the formulations were stable for 30 days at 40^{0}C and 75 % RH.

Table 1: Composition of Diltiazem hydrochloride fast dissolving tablets

Ingredients (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Diltiazem Hydrochloride	60	60	60	60	60	60	60	60	60
Crospovidone	3	6	9	-	-	-	-	-	-
Crosscarmellose Sodium	-	-	-	3	6	9	-	-	-
Sodium Starch Glycolate	-	-	-	-	-	-	3	6	9
Microcrystalline Cellulose	71	68	65	71	68	65	71	68	65
Mannitol	58	58	58	58	58	58	58	58	58
Orange Flavour	2	2	2	2	2	2	2	2	2
Talc	3	3	3	3	3	3	3	3	3
Magnesium Stearate	3	3	3	3	3	3	3	3	3
Total Weight	**200**	**200**	**200**	**200**	**200**	**200**	**200**	**200**	**200**

Table 2: Relationship between angle of repose ( ) and flow properties

Angle of repose ( ) (degrees)	Flow
<25	Excellent
25-30	Good
30-40	Passable
>40	Very Poor

Table 3: Percentage deviation in weight variation

Average weight of a tablet	Percentage deviation (%)
130 mg or less	10
More than 130 mg and less than 324 mg	7.5
324 mg or more	5

Table 4: Interpretation of IR graphs

Functional groups	Reported frequencies	Observed frequencies	
		Drug	Formulation
-C=C stretching	1700-1500	1680	1681.93
-NH stretching	3000-2800	2964.59	2916.37
-CH stretching	2400-2330	2353.16	2355.08
-C-H bending	1000-800	974.05	975.98

Table 5: Angle of repose, loose bulk density, tapped bulk density, compressibility index and Hausner's ratio

Formulation code	Angle of repose(θ)	Loose bulk density (gm/cm^3)	Tapped bulk density ($gm/cm^{3)}$	Compressibility Index (%)	Hausner's ratio
F1	27.10	0.45	0.54	17.68	1.19
F2	24.32	0.43	0.51	15.36	1.17
F3	22.48	0.40	0.49	14.82	1.15
F4	28.71	0.43	0.53	17.20	1.18
F5	26.39	0.42	0.51	16.47	1.18
F6	23.86	0.40	0.52	21.09	1.26
F7	28.37	0.42	0.52	20.87	1.21
F8	24.12	0.40	0.53	20.63	1.26
F9	22.55	0.39	0.50	23.01	1.31

Table 6: Thickness, hardness and friability

Formulation Code	Thickness* (n=3) (mm)	Hardness* (n=3) (Kg/cm^2)	Friability* % (n=10)
F1	4.01±0.02	3.48±0.25	0.71
F2	4.00±0.02	3.68±0.36	0.66
F3	4.01±0.04	3.01±0.48	0.57
F4	4.05±0.05	3.64±0.19	0.66
F5	4.05±0.05	3.46±0.31	0.59
F6	4.01±0.01	3.57±0.25	0.74
F7	4.05±0.02	3.73±0.57	0.67
F8	4.01±0.01	3.41±0.33	0.62
F9	4.01±0.03	3.58±0.62	0.58

*Represents value expressed as mean SD

Table 7: Drug content, weight variation and in-vitro disintegration time

Formulation code	Drug content* (n=5) (%)	Weight variation * (n=10) (mg)	Disintegration time* (sec)
F1	94.76±0.6	198±05	51±0.53
F2	96.02±0.8	197±04	47±0.41
F3	97.41±0.7	200±06	37±0.89
F4	93.53±0.6	197±03	53±0.46
F5	95.17±0.4	196±04	50±0.38
F6	96.44±0.9	197±05	44±0.61
F7	92.57±0.9	197±06	54±0.93
F8	94.61±0.3	198±06	48±0.87
F9	95.82±0.6	198±08	46±0.18

*Represents value expressed as mean SD

Table 8: Wetting time, water absorption ratio

Formulation code	Wetting time*(n=3) (sec)	Water absorption ratio* (n=3)
F1	56±1.35	79.71±0.19
F2	53±1.62	90.62±0.30
F3	42±1.45	95.48±0.41
F4	58±1.91	76.83±0.20
F5	55±1.76	78.20±0.31
F6	47±1.41	84.94±0.52
F7	59±1.53	76.21±0.79
F8	57±1.68	88.41±0.37
F9	50±1.29	91.63±0.88

*Represents value expressed as mean SD

Table 9: *In-vitro* dissolution studies

Formulation code	After 3 min % release	After 6 min % release	After 9 min % release	After 12 min % release	After 15 min % release
F1	42.34	60.75	76.26	80.68	84.46
F2	43.67	62.59	78.28	82.05	86.00
F3	46.01	64.44	79.97	84.41	91.72
F4	40.00	60.07	75.58	79.66	83.27
F5	41.17	61.41	77.09	80.52	83.80
F6	43.17	63.42	78.12	83.05	88.17
F7	39.67	58.57	75.07	79.15	82.25
F8	41.84	61.25	76.93	79.69	83.13
F9	44.01	62.26	78.78	82.88	88.51

Table 10: Stability studies for optimized formulation (F3) stored at 40^0C/ 75 %RH after 30 days

Formulation code	Thickness (mm)	Hardness (Kg/cm^2)	Drug content (%)	Drug release (%)
F3	4.00±0.01	3.01±0.25	97.41±0.1	91.41

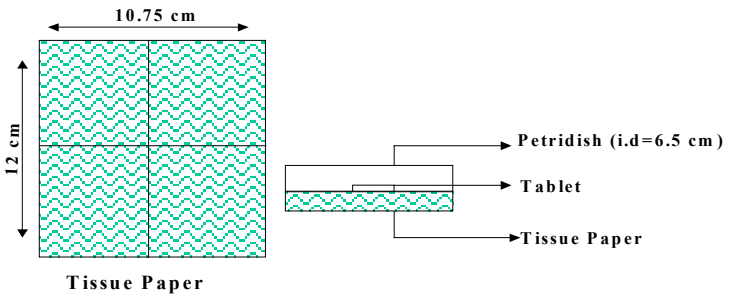

Figure 1: Simple method for the measurement of wetting time of a tablet

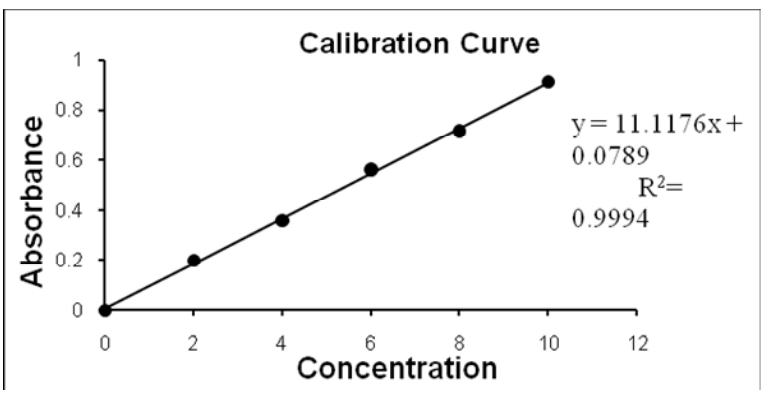

Figure 2: Standard calibration curve of Diltiazem hydrochloride at 237 nm in phosphate buffer (pH 6.8)

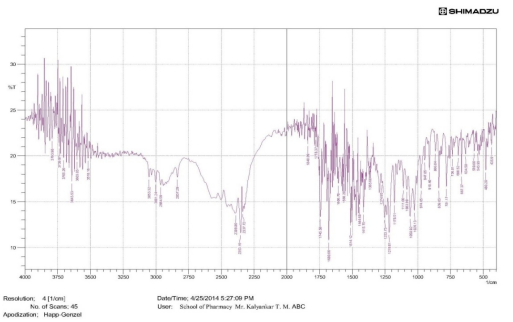

Figure 3: IR spectra of Diltiazem hydrochloride

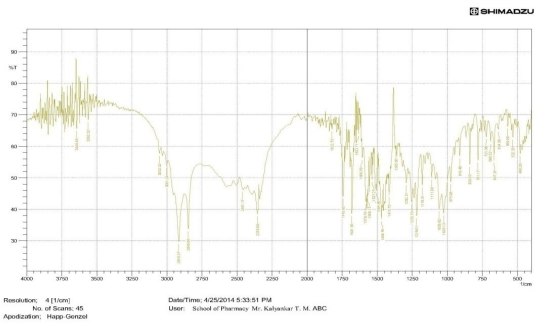

Figure 4: IR spectra Drug and excipients

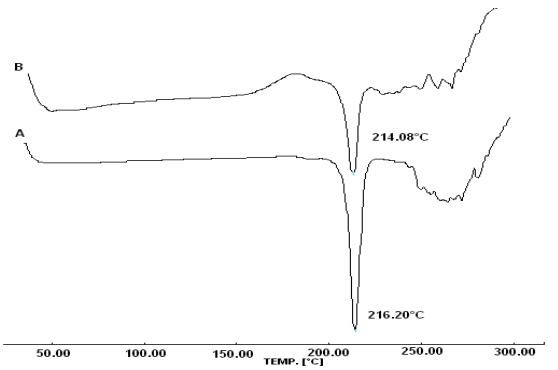

Figure 5: Overlain DSC of A) pure drug Diltiazem hydrochloride and B) optimized formulation F3

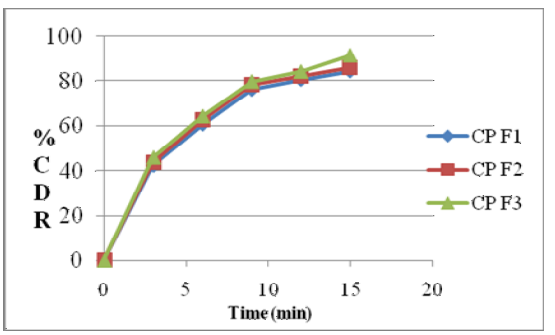

Figure 6: Comparative *in-vitro* release profiles of Diltiazem hydrochloride fast dissolving tablets for formulations F1, F2, F3

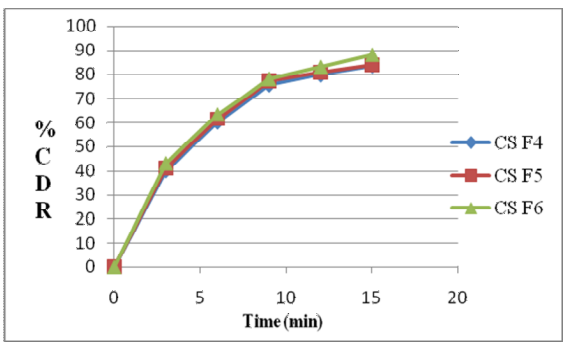

Figure 7: Comparative *in-vitro* release profiles of Diltiazem hydrochloride fast dissolving tablets for formulations F4, F5, F6

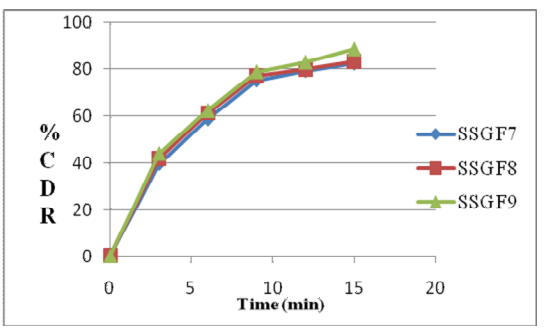

Figure 8: Comparative *in-vitro* release profiles of Diltiazem hydrochloride fast dissolving tablets for formulations F7, F8, F9

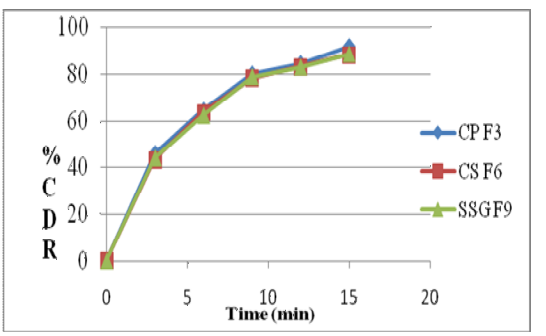

Figure 9: Comparative *in-vitro* release profiles of Diltiazem hydrochloride fast dissolving tablets for formulations F3, F6, F9

ACKNOWLEDGEMENT

Authors were thankful to Balaji Drugs, Gujarat, India for providing gift sample of Diltiazem hydrochloride. We would also like to thanks Principal and Management of Sahyadri College of Pharmacy, Methwade, Sangola, Solapur, Maharashtra, India for providing all the facilities to complete this work successfully.

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Cite this article as:

Doke Onkar, Patil Manojkumar, Tamboli Dilshadbee, Mali Audumbar, Hake Gorakhnath. Development and evaluation of fast dissolving tablets of diltiazem hydrochloride. Int. J. Res. Ayurveda Pharm. 2015;6(4):493-501 http://dx.doi.org/10.7897/2277-4343.06494

Source of support: Nil, Conflict of interest: None Declared