ORIGINAL ARTICLE

Development and evaluation of diltiazem hydrochloride controlled-release pellets by fluid bed coating process

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ABSTRACT

The aim of the present study was to develop controlled-release pellets of diltiazem HCl with ethyl cellulose and hydroxylpropyl methylcellulose phthalate as the release rate retarding polymers by fluid bed coating technique. The prepared pellets were evaluated for drug content, particle size, subjected to Scanning Electron Microscopy (SEM) and Differential Scanning Calori metry (DSC), and evaluated for *in vitro* release. Stability studies were carried out on the optimized formulations for a period of 3 months. The drug content was in the range of 97%-101%. The mean particle size of the drug-loaded pellets was in the range 700-785 μm. The drug release rate decreased as the concentration of ethyl cellulose increased in the pellet formulations. Among the prepared formulations, FDL10 and FDL11 showed 80% drug release in 16 h, matching with USP dissolution test 6 for diltiazem HCl extended-release capsules. SEM photographs confirmed that the prepared formulations were spherical in nature with a smooth surface. The compatibility between drug and polymers in the drug-loaded pellets was confirmed by DSC studies. Stability studies indicated that the pellets were stable.

Key words: Controlled release, diltiazem HCl, fluid bed coating, multiparticulate dosage forms, sustained release

INTRODUCTION

Multiparticulate dosage forms (MPDFs) are receiving an immense attention as alternative drug delivery systems for oral drug delivery even though single-unit dosage forms have been widely used for decades. The most commonly used pharmaceutical solid dosage forms today include granules, pellets, tablets, and capsules, out of which tablets are the most popular dosage form, accounting for 70% of all ethical pharmaceutical preparations produced.

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The most interesting area in the development of MPDFs is incorporation into tablets instead of hard gelatin capsules in order to make them more economical to the consumers, and is gaining more attention currently. The present research work focuses on the pelletized form of multiple units; they are prepared by a process called pelletization which is referred to as a size enlargement process and the final products obtained are called pellets. Pellets provide a reduction in the dosage regimen and gastrointestinal (GI) irritation. They increase the absorption of the active ingredient and possess controlled drug release properties. Also, one of the advantageous properties of the pellet formulations is them being good candidates for the delivery of the drug substances by minimizing the dose-dumping effect. The reproducibility of the release characteristics from pellet formulations is also much better with respect to the single-unit dosage forms. They are suitable systems for film coating with respect to the high surface area–volume ratios. Also, resistance to external factors such as moisture, air, and light is the most advantageous property of these dosage forms.[1-4]

In the present study, fluid bed coating (FBC) process was employed for the preparation of diltiazem HCl pellets. Fluidized bed processor is an equipment that can perform multiple functions like coating, drying, granulation, and pelletizing. It is applied for specific manipulation of the particle surface characteristics.[5-7]

Diltiazem HCl is a calcium channel blocker which is widely used in the treatment of variant angina, hypertension, and supraventricular tachyarrhythmias. It is freely soluble in distilled water, chloroform, and methanol. Diltiazem HCl is rapidly absorbed (90%) after oral administration, but availability is only 30%-40% in systemic circulation and bioavailability varies between individuals. It has an elimination half-life of 3-5 h and is slightly prolonged after multiple dosing.[8] Based on the above physical, chemical, biopharmaceutical properties and clinical relevance, diltiazem HCl was selected as the drug candidate for developing controlled release pellet formulations.

The controlled release pellets of diltiazem HCl with ethyl cellulose and hydroxylpropyl methylcellulose phthalate (HPMCP) by employing fluid bed coating technique. Ethyl cellulose 7 cps, a high-viscosity grade polymer, was used for regulating the drug release from the pellet formulations. HPMCP, an enteric coating polymer, was used in the present study to regulate the drug release at varied GI pH conditions. An attempt was made to optimize the composition of these two polymers to achieve the controlled release of drugs from the pellets. Pellets offer a great flexibility in pharmaceutical solid dosage form design and development. They are better than other dosage forms in terms of ease of coating, sustained, controlled, or site-specific delivery of the drug from coated pellets, uniform packing, even distribution in the GI tract, and less GI irritation.[9] HPMC E5 was used as a film former in the present investigation. Croscarmellose sodium was used as the disintegrant to create channels in the coating for drug release. Povidone was used as the binder to achieve uniform drug layering in the present study.[10,11]

MATERIALS AND METHODS

Materials

Diltiazem HCl was obtained as a gift sample from Pellet Pharma Ltd., Hyderabad, India. The excipients povidone K-30 and ethyl cellulose (EC) 7 cps were obtained as gift samples from Pellet Pharma Ltd., and HPMC E5 was obtained as a gift sample from Dow Chemicals Asia Pvt., Ltd., Mumbai, India. HPMC phthalate, talc, isopropyl alcohol, and propylene glycol were obtained as gift samples from Lobachemi Pvt. Ltd., Mumbai, India.

Preparation of Diltiazem HCL Release Pellets by Fluid Bed Coating

Equal quantities of diltiazem HCl and croscarmellose sodium were taken in a bowl and mixed with gloved hand. To the mixture, another equivalent quantity of diltiazem HCl was added and mixed with help of gloved hand, and the remaining quantity of drug was loaded into the blender and mixed with the powder for 10 min.

Preparation of povidone solution

Isopropyl alcohol, PVP K-30 (polyvinyl pyrrolidone), and Tween 80 were taken into stainless steel propeller-type stirrer mixer and mixed for 10 min. The solution was filtered through nylon cloth into SS tank.

Drug Loading

Sugar pellets were charged into fluidization basket. The drug and croscarmellose powder blends were also charged into the fluidized basket and povidone solution was atomized onto the materials while the air was allowed to circulate into the basket at an air flow rate of 2000-4500 cfm to keep the materials under fluidized state. The process of fluidization was continued for 10 min. The drug-loaded pellets from the FBC were spread into the trays uniformly and dried at 60°C temperature for about 3 h. After drying, the pellets were sifted by using vibro sifter to remove the fines and to separate the uniform-sized pellets.

Preparation of HPMC E5 Solution

HPMC E5 and water were taken into the stainless steel tank and mixed for 10 min with propeller-type stirrer. The solution was filtered through nylon cloth into SS tank.

Sub-Coating

The drug-loaded pellets were charged into fluidization basket. HPMC E5 polymer solution was atomized onto the materials while the air was allowed to circulate into the basket at an air flow rate of 2000-4500 cfm to keep the materials under fluidized state. The process of fluidization was continued for 10 min. Coating of the pellets was done under specified conditions like inlet temperature of 40°C and outlet temperature of 35°C, with an air pressure 2.5 kg/cm^2. Damper was adjusted such that pellets should not hit the upper screen. Flow rate rpm was adjusted to 18-22 rpm. The drug-loaded pellets from the FBC were spread onto the trays uniformly and dried at 60°C temperature for about 3 h. After drying, the pellets were sifted by using vibro sifter to remove fines and the uniform-sized pellets were collected.

Preparation of HPMCP Solution

HPMCP, cetyl alcohol, acetone, and isopropyl alcohol were taken into the tank and mixed for 10 min at 1300 rpm by using propeller-type stirrer and filtered through nylon cloth into SS tank.

Polymer Loading

The HPMC-coated pellets were charged into fluidization basket. Polymer solution was atomized onto the materials while the air was allowed to circulate into the basket at an air flow rate of 2000-4500 cfm to keep the materials under fluidized state. The process of fluidization was continued for 10 min. Pellets were coated under specified conditions like inlet temperature of 40°C and outlet temperature of 35°C, with an air pressure of 2.5 kg/cm^2. Damper was adjusted

such that pellets should not hit the upper screen. Flow rate rpm was adjusted to 24-28 rpm. The drug-loaded pellets from the FBC were spread onto the trays uniformly and dried at 60°C temperature for about 3 h. After drying, the pellets were sifted by using vibro sifter to remove fines and the uniform-sized pellets were collected.

Preparation of EC Solution

Ethyl cellulose, diethyl phthalate, talc, Isopropyl Alcohol (IPA) and acetone were taken into the SS tank. They were mixed in a homogenizer for 15 min and filtered through nylon cloth into SS tank.

Polymer Loading

The HPMCP-coated pellets were charged into fluidization basket. EC polymer solution was atomized onto the materials while the air was allowed to circulate into the basket to keep the materials under fluidized state. The process of fluidization was continued for 10 min. The fluid bed coating process variables were given in the Table 1.

Finally the coated pellets were dried at ambient conditions for 2 h and sifted through vibro sifter to collect uniform-sized pellets. The composition of various diltiazem hydrochloride controlled release pellets is given in Table 2.

Table 1: Fluid bed coating process variables

Process controls	Specifications
Batch size	500 G
Inlet air temperature	40°C
Outlet air temperature	35°C
Product temperature	35°C
Chamber humidity	60% RH
Air flow	2000-4500 cfm
Nozzle aperture	1.2 mm
No. of spray guns	1
Spray direction	Bottom spray
Spray pressure	2.5 kg/cm^2
Spray time	10 min
Secondary drying	60°C

Evaluation of Physical Parameters

Percentage Yield

All the batches of controlled-release diltiazem pellets prepared by fluid bed coating were evaluated for percentage yield of the pellets. The actual percentage yields of pellets were calculated by using the following formula. The % yields of various batches of pellets are given in Table 3.

$$\text{Percentage yield of pellets} = \frac{\text{Practical yield of pellets}}{\text{Theoretical yield of pellets}} \times 100$$

Particle Size Determination

The average particle size of the pellet formulations of diltiazem hydrochloride was analyzed by simple sieve analysis method. The particle size of various batches of pellets is given in Table 3.

Friability

The friability of the core pellets of diltiazem hydrochloride[12] was determined as % weight loss after 100 revolutions of 10 g of pellets in a friabilator. The friability values of various pellets formulations are given in Table 3.

Drug Content

One gram of diltiazem hydrochloride pellets from each batch was taken at random and crushed to a fine powder. The powdered material was transferred into a 100 ml volumetric flask and 70 ml of distilled water was added to it. It was shaken occasionally for about 30 min and the volume was made up to 100 ml by adding distilled water. About 10 ml of the solution from the volumetric flask was taken and centrifuged. The solution from the centrifuge tube was collected and again filtered by using Millipore filter. Then the filtrate was subsequently diluted and the absorbance was measured at 238 nm for diltiazem hydrochloride. This test

Table 2: Composition of various diltiazem HCl pellets prepared by fluid bed coating

Ingredients for 10 g	FDL1	FDL2	FDL3	FDL4	FDL5	FDL6	FDL7	FDL8	FDL9	FDL10	FDL11
Diltiazem HCl	5.728	5.728	5.728	5.728	5.728	5.728	5.728	5.728	5.728	5.728	5.728
Povidone	0.376	0.376	0.376	0.376	0.376	0.376	0.276	0.276	0.276	0.276	0.276
Ethyl cellulose	0.010	0.012	0.014	0.016	0.018	0.020	0.020	0.020	0.020	0.020	0.020
HPMC E_5	0.240	0.240	0.240	0.240	0.240	0.240	0.240	0.240	0.240	0.240	0.240
HPMC phthalate	0.020	0.020	0.020	0.020	0.020	0.020	0.010	0.012	0.014	0.016	0.018
Cetyl alcohol	0.015	0.015	0.015	0.015	0.015	0.015	0.015	0.015	0.015	0.015	0.015
Diethyl phthalate	0.016	0.016	0.016	0.016	0.016	0.016	0.016	0.016	0.016	0.016	0.016
Acetone	2.308	2.308	2.308	2.308	2.308	2.308	2.308	2.308	2.308	2.308	2.308
IPA	5.543	5.543	5.543	5.543	5.543	5.543	5.543	5.543	5.543	5.543	5.543
Talc	0.037	0.037	0.037	0.037	0.037	0.037	0.037	0.037	0.037	0.037	0.037
Croscarmellose sodium	0.055	0.055	0.055	0.055	0.055	0.055	0.056	0.056	0.056	0.056	0.056
Sugar spheres	3.518	3.518	3.518	3.518	3.518	3.518	3.518	3.518	3.518	3.518	3.518
Purified water	1.847	1.847	1.847	1.847	1.847	1.847	1.847	1.847	1.847	1.847	1.847
Tween-80	0.027	0.027	0.027	0.027	0.027	0.027	0.027	0.027	0.027	0.027	0.027

Table 3: Physical parameters of diltiazem HCl pellets by fluid bed coating

Formulations	% Yield	Average pellet particle size (μm)	Friability %	Drug content
FDL1	91.5±0.2	702±20	0.085	98.2±0.3
FDL2	92.6±0.6	733±25	0.084	97.6±0.6
FDL3	91.6±0.5	726±16	0.092	99.5±0.4
FDL4	93.9±0.2	745±24	0.087	101.9±0.2
FDL5	90.2±0.2	785±34	0.089	98.2±0.5
FDL6	94.8±0.3	756±24	0.094	99.8±0.4
FDL7	92.7±0.4	756±27	0.098	97.7±0.4
FDL8	92.4±0.3	776±29	0.092	99.4±0.3
FDL9	92.8±0.5	758±21	0.096	101.8±0.5
FDL10	92.6±0.2	781±19	0.084	98.6±0.4
FDL11	94.8±0.3	756±24	0.086	99.8±0.4

was repeated six times ($N = 6$) for each batch of pellets. The drug content of various batches of pellets is given in Table 3.

In Vitro Dissolution Studies

One hundred and twenty milligram equivalent weight of diltiazem hydrochloride containing pellets was collected and weighed at random from each batch of pellet formulation and dissolution studies were performed in a calibrated 8-station dissolution test apparatus (Disso 2000) equipped with paddles (USP apparatus II method),[13] employing 900 ml of distilled water as the medium. The paddles were operated at 100 rpm and the temperature was maintained at 37 ± 1°C throughout the experiment. Five milliliter of the samples was withdrawn at regular intervals up to 24 h and replaced with an equal volume of fresh dissolution medium to maintain a constant volume of the dissolution medium throughout the experiment. Samples withdrawn at various time intervals were suitably diluted with the same dissolution medium and the amount of drug released was estimated by ELICO double-beam spectrophotometer at 238 nm. The dissolution studies on each formulation were conducted three times. Necessary corrections were made for the loss of drug due to each sampling.

The dissolution profiles of all the pellet formulations of diltiazem hydrochloride were compared with the marketed extended-release pellet formulation of diltiazem hydrochloride by using a model-independent approach of similarity factor *f*2, with all time points included in the *in vitro* dissolution studies.[14,15] The equation for calculating similarity factor is:

$$f2 = 50 \times \log\left\{\left[1 + (1/n)\sum_{J=1}^{N} |Rt\ Tt|^2\right] - 0.5 \times (100)\right\}$$

where "*n*" is the number of dissolution time and R_t and T_t are the reference (theoretical) and test dissolution values at time "*t*," respectively. Dissolution profile was considered satisfactory if *f*1 value was below 15 (nearing zero) and *f*2 value was more than 50. Two dissolution profiles were considered similar when the *f*2 value was 50–100.

Characterization of Pellets

The selected formulations were subjected to Differential Scanning Calorimetry (DSC) studies to identify any possible interaction between drug and polymers during the coating process. The surface characteristics of the pellets were determined by Scanning Electron Microscopy (SEM) analysis.

Accelerated Stability Studies

The formulations which showed good *in vitro* performance (FDL10 and FDL11) were subjected to stability studies under accelerated temperature and relative humidity (RH) conditions (40°C and 75% RH) for 3 months. Test samples withdrawn after 3 months were subjected to various tests, including visual inspection for any appreciable change on the pellet surface, assay, and dissolution.

RESULTS AND DISCUSSION

Diltiazem HCl pellets were prepared by fluid bed coating process. All batches of pellet formulations were formulated and manufactured under identical conditions by maintaining specific process parameters which are given in Table 1. The compositions of various pellet formulations are shown in Table 2. The pellet formulations were evaluated for physical parameters such as % yield, particle size, friability, and drug content. The percent yields of various coated pellets were in the range of 90%-95%, and the particle size of all the batches of pellets were in the range of 700-785 μm. The friability loss of the coated pellets was less than 0.1%, and the percent of drug present in various pellet formulations was found to be in the range of 97%-102%. All the physical parameters evaluated for the various batches of pellet formulations are given in Table 3. Dissolution studies were performed on all the controlled-release pellets by using USP paddle method (apparatus II). The dissolution profiles of all the pellet formulations are shown in Figures 1 and 2. The drug release from the pellet formulations was extended up to 18 h in majority of the formulations. Formulations FDL1-FDL4 extended the drug release up to 14 h. Formulations FDL5-FDL11 extended the drug release up to 18 h. The drug release rate decreased as the concentration of ethyl cellulose increased in the formulations. Remaining formulations extended the drug release up to 16 h. Among the prepared formulations, FDL10 and FDL11 showed drug release up to 80% at the end of 16 h, matching with USP dissolution test 6[12] for diltiazem HCl extended-release capsules. It was observed that increase in the concentration of ethyl cellulose resulted in delay of the drug release from the pellets. The increase in HPMCP concentration in

formulations showed initial delay in drug release, i.e. up to 4 h, and further the rate of release was increased. All the pellet formulations were found to be linear with first-order release rate with R^2 values in the range of 0.988–0.998, indicating that the rate of drug release from all the pellet formulations was concentration dependent. The Higuchi's plots for all the pellet formulations were found to be linear with R^2 values in the range of 0.969-0.998. The release exponent values (n values) for all the pellet formulations were in the range of 0.52-0.81, indicating that the drug release was by non-Fickian diffusion. Thus, the drug release from the pellet formulations was by diffusion of the drug from the polymeric matrix, followed by erosion of the polymer. The *in vitro* dissolution parameters were shown in the Table 4. The dissolution profiles of diltiazem hydrochloride pellet formulations were compared with those of the marketed controlled release formulation of diltiazem hydrochloride extended-release pellets. The similarity factors were calculated for these formulations. The similarity factor f_2 values were in the range of 19-89. The formulations FDL10 and FDL11 showed the similarity factor values above 50, indicating that the release profiles for these formulations were similar to that of marketed formulation. DSC analysis was performed for the pure drug and selected pellet formulations to study the drug excipient interactions.

A broad endothermic peak at 214.80°C was observed for the pure drug diltiazem, which is the characteristic peak for diltiazem HCl.[16] For the formulations FDL6 and FDL12, the broad endothermic peaks were observed at 213.44°C and 215.66°C. The results revealed that there was no major

Table 4: *In vitro* dissolution parameters of diltiazem hydrochloride pellets by fluid bed coating

Formulation	First-order constant		Higuchi constants		Peppas constant	
	K (h^{-1})	R^2	K ($mg^{1/2}$)	R^2	*N*	R^2
FDL1	0.272	0.999	32.34	0.987	0.52	0.998
FDL2	0.227	0.994	31.46	0.978	0.56	0.987
FDL3	0.177	0.991	29.95	0.981	0.69	0.984
FDL4	0.161	0.994	29.27	0.993	0.69	0.991
FDL5	0.126	0.991	26.34	0.985	0.66	0.996
FDL6	0.112	0.988	26.16	0.969	0.81	0.997
FDL7	0.337	0.996	26.77	0.986	0.55	0.999
FDL8	0.253	0.990	26.07	0.978	0.62	0.995
FDL9	0.204	0.998	27.18	0.989	0.65	0.992
FDL10	0.166	0.995	27.54	0.998	0.68	0.987
FDL11	0.148	0.990	27.02	0.998	0.81	0.988

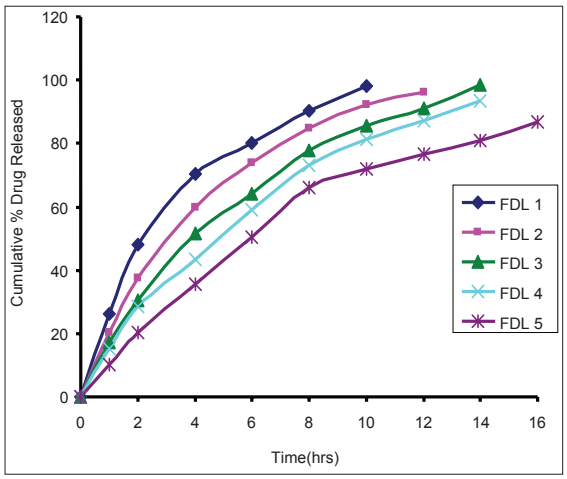

Figure 1: Drug release profiles for controlled-release diltiazem hydrochloride pellets

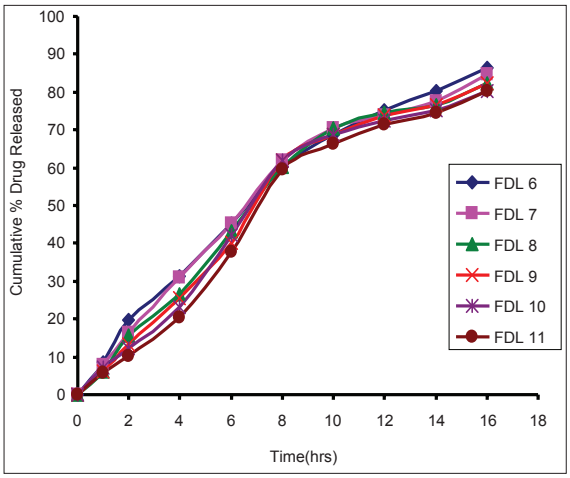

Figure 2: Drug release profiles for controlled-release diltiazem hydrochloride pellets

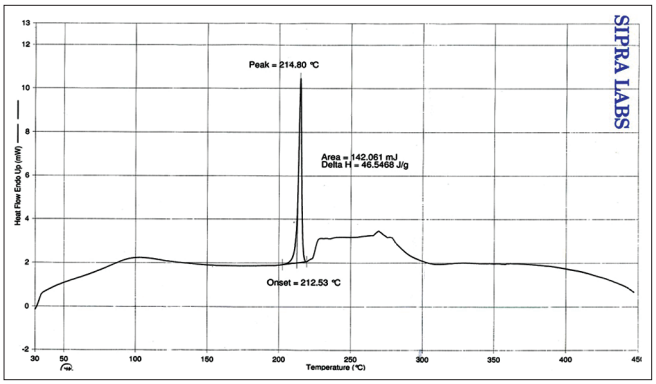

Figure 3: DSC thermograph of pure diltiazem HCl drug

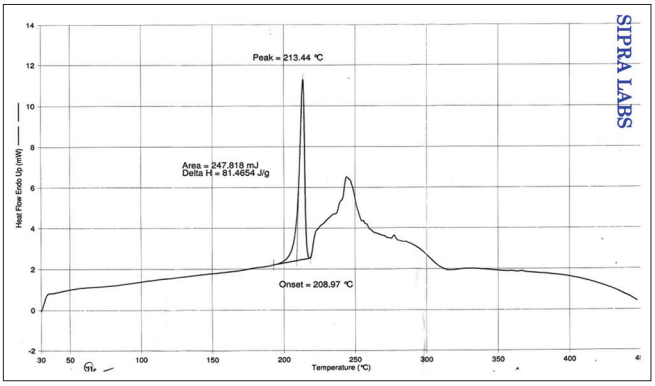

Figure 4: DSC thermograph of diltiazem HCl pellets (FDL6)

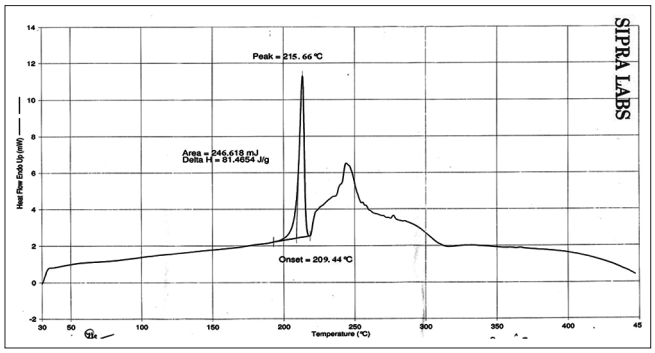

Figure 5: DSC thermograph of diltiazem HCl pellets (FDL12)

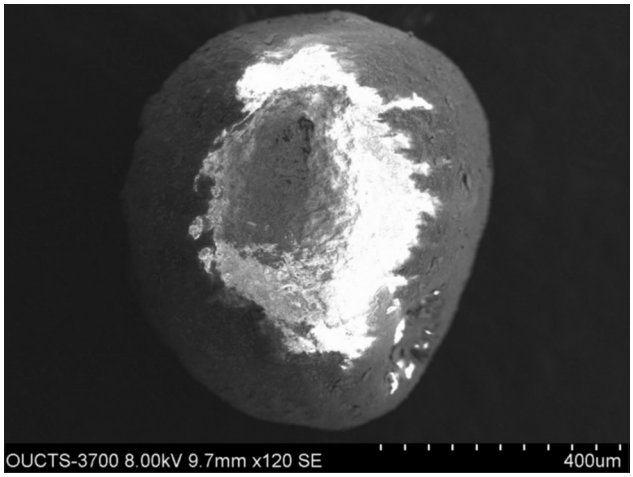

Figure 7: SEM images of diltiazem HCl pellets

interaction between the drug and the polymers during the coating process. The DSC endotherms are shown in Figures 3-5.

Optimized pellet formulations were characterized by SEM analysis to understand the pellet surface morphology. The pellets prepared by FBC were having smooth surface with minimal pores, indicating the uniform coating of the pellets. The SEM images of the pellet formulations are shown in Figures 6 and 7.

The optimized pellet formulation was further evaluated by accelerated stability studies. The stability studies indicated that there were no visible and physical changes observed in the pellet formulations after storage at accelerated conditions. The drug-release characteristics of the pellets remained unaltered after 3 months of storage. The dissolution profiles of the formulations FDL10 and FDL11 before storage and after storage (FDL10S and FDL 11S) are shown in Figure 8.

CONCLUSIONS

The multi-unit dosage form pellets that were formulated by fluid bed coating process showed controlled release of diltiazem hydrochloride for a prolonged period of time.

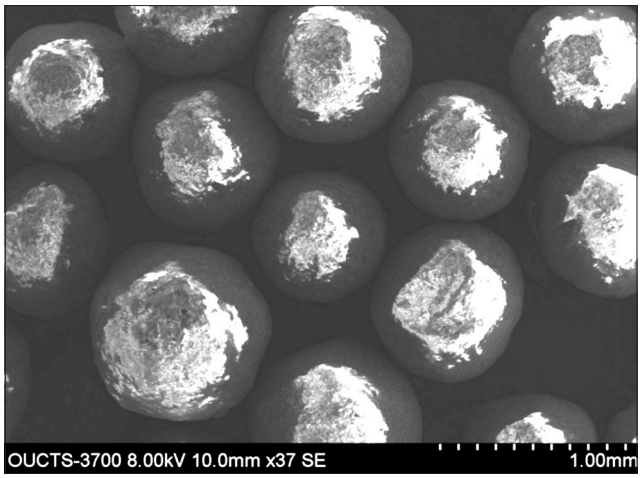

Figure 6: SEM images of diltiazem HCl pellets

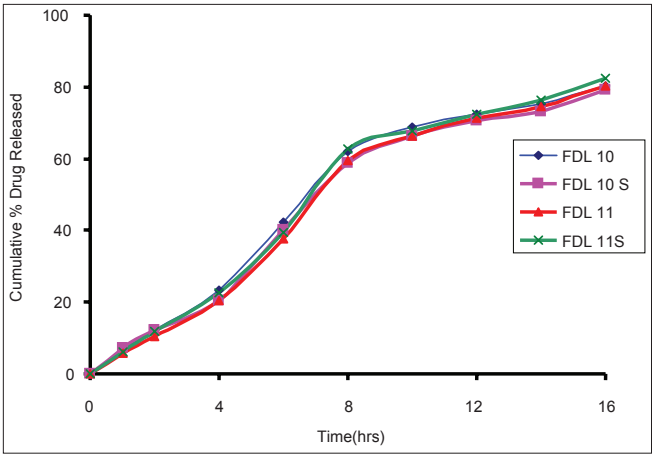

Figure 8: Drug release profiles diltiazem hydrochloride pellets before and after storage

Based on the results, the pellets prepared by FBC process were found to be ideal for the preparation of diltiazem hydrochloride controlled-release formulations.

REFERENCES

1. Jagadeesh T, Bala Ramesha CR. Development of a novel oral Multi Particulate Drug Delivery System of Galantamine hydrobromide. J Pharm Res 2011;4:77-9.
2. Jagdale SC, Chede SM, Gulwady R, Kuchekar BS, Lokhande PD, Shah TP, *et al*. Pulsatile multiparticulate drug delivery system for metoprolol succinate. Arch Pharm Res 2011;34:369-76.
3. Singh G, Pai RS, Devi VK. Response surface methodology and process optimization of sustained release pellets using Taguchi orthogonal array design and central composite design. J Adv Pharm Technol Res 2012;3:30-40.
4. Tripude RN, Puranik PK. Rabeprazole sodium delayed-release multiparticulates: Effect of enteric coating layers on product performance. J Adv Pharm Technol Res 2011;3:184-91.
5. Wesdyk R, Joshi YM, Jain NB, Morris K, Newman A. The effect of size and mass on the film thickness of beads coated in fluidized bed equipment. Int J Pharm 1990;65:69-76.
6. Nastruzzi C, Cortesi R, Esposito E, Genovesi A, Spadoni A,

Vecchio C, *et al*. Influence of formulation and process parameters on pellet production by powder layering technique. AAPS Pharm Sci Tech 2000;1:E9.
7. Laicher A, Lorck CA, Tobin J, Stanilaus F. Process optimization of pellet coating and drying using fluidbed production units. Pharm Tech Eur 1994;8:41-8.
8. Reynolds JE, Martindale. The Extra Pharmacopoeia. Vol. 30. London: The Pharmaceutical Press; 1993. p. 354-7.
9. Kammili L, Senthil V, Varun R. Pelletization technology: A quick review. Int J Pharm Sci Res 2011;2:1337-55.
10. Raymond CR. Handbook of Pharmaceutical Excipients. 6th ed. UK: Pharmaceutical Press; 2009.
11. Botzolakis JE, Augsburger LL. Disintegrating agents in hard gelatin capsules. Part I: Mechanism of action. Drug Dev Ind Pharm 1988;14:29-41.
12. Santos H, Veiga F, Pina M, Podczeck F, Sousa J. Physical properties of chitosan pellets produced by extrusion-spheronisation: Influence of formulation variables. Int J Pharm 2002;246:153-69.
13. United States Pharmacopoeia. Diltiazem Hydrochloride Extended-Release Capsules monograph. Rockville, Maryland, USA, 27th ed. 2004. p. 1953-55.
14. Quality control. 4th ed. Pharmaceutical statistics: Practical and clinical applications. In: Bolton S, Bon C, editors. New York: Marcel Dekker; 2004. p. 408-11.
15. Moore JW, Flanner HH. Mathematical comparison of dissolution profiles. Pharm Tech 1996;20:64-74.
16. Shivanand P, Viral D, Manish G, Shailesh K. Formulation, characterization and *in vitro* evaluation of Diltiazem Hydrochloride matrix tablets. Der Pharmacia Lett 2010;2:482-8.

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