RESEARCH ARTICLE

Design, Development and Evaluation of Telmisartan and Azelnidipine Loaded Multiparticulate Pulsatile Drug Delivery System

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ABSTRACT

This study aimed to design, develop, and assess multiparticulate pulsatile drug delivery for the chronotherapeutic administration of Azelnidipine and Telmisartan. PVP K- 30 has been employed as a binder in the result layering fashion for manufacturing the drug- loaded bullets (pallets). The polymer affect amalgamation of Eudragit RS 100 and RL 100 at varying composition was applied to the drug- loaded peerless globules using a amalgamation of IPA:DCM (7:3), triethyl citrate (TEC) as a plasticizer, and talc as an anti-sticking agent. The set bullets (pellets) were also estimated for FTIR, Flow properties, friability, medicine (drug) content, SEM and *in vitro* dissolution study. FTIR study reveals no commerce between drug and polymer. SEM study vindicated the smooth appearance of coating over the surface of pellets. Pallets carpeted with 10% polymer coating weight gain showed promising lag-time and detention drug release. Batch F6 prepared with 60:40 rate of eudragit RS and RL 100 polymer gives total lag time of 4 hrs and drug release in 8 hr. The stability of the farther bettered carpeted pellet expression was excavated. After three months of storage at 45 °C/ 75% RH, expression F7 was set up to have no distinguishable changes in its physical appearance, drug content, or *in- vitro* dissolution pattern.

Keywords: Telmisartan, Azelnidipine, Eudragit, Solution Layering technique, Pulsatile Drug delivery system, etc.

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Conflict of interest: None

INTRODUCTION

Conventional drug delivery systems release medication at a constant rate, which often does not align with the body's natural pattern and fluctuating needs. This can lead to periods of over- or under-medication, potentially causing side effects or reduced efficacy, particularly for conditions like hypertension that follow a circadian pattern[1,2]. Hence there is need of special type of drug delivery system like pulsatile drug delivery systems (PDDS) which release drugs in a controlled, time-specific manner, matching the body's natural rhythms. This method enhances therapeutic efficacy and reduces side effects by delivering drugs at the optimal time, particularly for diseases following circadian patterns, such as asthma, arthritis, and cardiovascular disorders[3]. PDDS improves patient compliance by reducing the frequency of dosing and minimizing the risk of drug tolerance. Additionally, these systems can protect drugs from degradation in the gastrointestinal tract and target drug release to specific sites within the body, maximizing the therapeutic benefits and minimizing systemic exposure. Pulsatile drug delivery systems (PDDS) are particularly important in managing hypertension due to their ability to align drug release with the body's circadian rhythms. Pressure exerted by the blood on the walls or arteries usually follows a daily rhythm, raising in the early morning and late afternoon. PDDS can deliver antihypertensive medication at these critical times, enhancing therapeutic efficacy and better controlling blood pressure fluctuations. This targeted delivery reduces the risk of adverse effects and improves patient compliance by potentially reducing the number of doses required. Moreover, by mimicking the body's natural rhythm, PDDS minimizes the risk of morning surge hypertension, a significant predictor of cardiovascular events[4,5].

Multiparticulate pulsatile drug delivery systems consist of multiple small, discrete units such as pellets, granules, or mini-tablets, each designed to release the drug at specific times. These units can be coated with polymers that dissolve at different rates or in response to specific triggers, ensuring timed, controlled drug release. This approach offers several benefits, including reduced risk of dose dumping, improved drug absorption, and enhanced flexibility in achieving desired release profiles[6]. This research was aimed to developed the multiparticulate PDDS loaded with Telmisartan and Azelnidipine for the chorotheraphy of hypertension. Telmisartan is angiotensin II receptor blockers and Azelnidipine is a calcium channel blocker, both drugs are ubiquitously utilized for the management and treatment of hypertension in combination.

MATERIALS AND METHODS

Telmisartan was obtained as gift sample from (Vasudha Pharma Chem ltd. Visakapatnam) Ajanta Pharma Limited, Chitegaon, Chhatrapati Sambhajinagar, India. Azelnidipine

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I.P. (Micronized) was supplied as gift sample by IPCA laboratories, Mumbai India. Eudrgit RS 100, RL 100 and all excipients were taken from Research center P. Wadhwani college of Pharmacy, Yavatmal. All other solvents and materials are of analytical grade.

Preparation of Drug Loaded Pellets of Telmisartan and Azelnidipine

Solution layering technique was utilized for the preparation of drug loaded pellets. Solution mixture of drug telmisartan and azelnidipine (40 mg and 8 mg per dose) was prepared in solvent mixture of IPA and water in the ratio of (80:20). PVP K-30 (2%) was added as a binder in the above mixture. The solution was then sprayed onto the rotating nonpareil seeds in laboratory coating pan at the flow rate of 1 ml/min, so as to prevent the agglomeration of pellets during coating process. The inner air temperature was maintained at 45°C. After each application of solution mixture the drying time 2 min was utilized. The speed of coating pan was maintained 25 rpm throughout the process. The layering process was continued till all the drug solution was applied on surface of pellets. The drug-loaded pellets were finally dried in oven at 70°C for 30 min. Composition of drug loaded Pellets were given in (Table 1)[7,8].

Table 1: Composition of drug loaded Pellets

S. No.	Ingredients	Mg/Capsules
1	Nonpareil seeds	450
2	Telmisartan	40
3	Azelnidipine	8
4	PVP K30	9
	Total	507

Formulations of Coated Pellets

The drug loaded nonpareil beads were coated by use of polymeric solution mixture of two grades of Eudragit RS 100 and RL 100. Table 2 shows the composition in details. A fixed concentration of eudragit polymer (5%) having different composition was prepared and utilized. Polymeric mixture was prepared by dissolving it in IPA: DCM (7:3) mixture. The polymeric solution was plasticized by triethyl citrate (TEC) 15 %, w/w based on polymer weight and talc was added as antisticking agent (5% w/w) related to dry polymer weight. Required quantities of drug loaded pellets were loaded to the coating pan and were coated with polymeric solution. During the coating process the flow rate coating solution was maintained at 1 ml/min. The inlet drying temperature was maintained at 45°C. Drying time

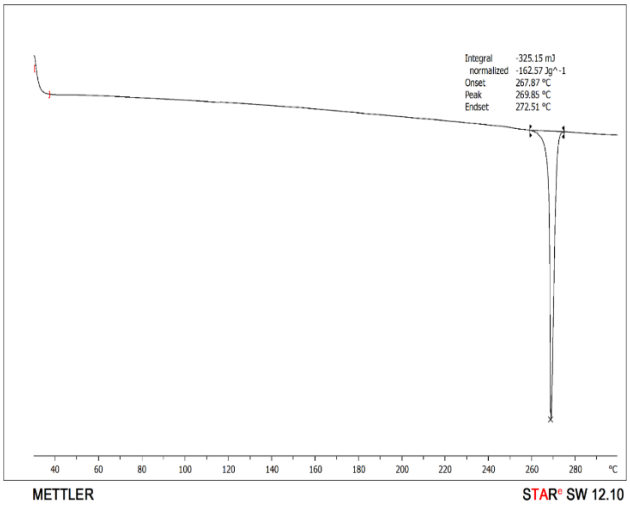

Figure 1: DSC Thermogram of Telmisartan

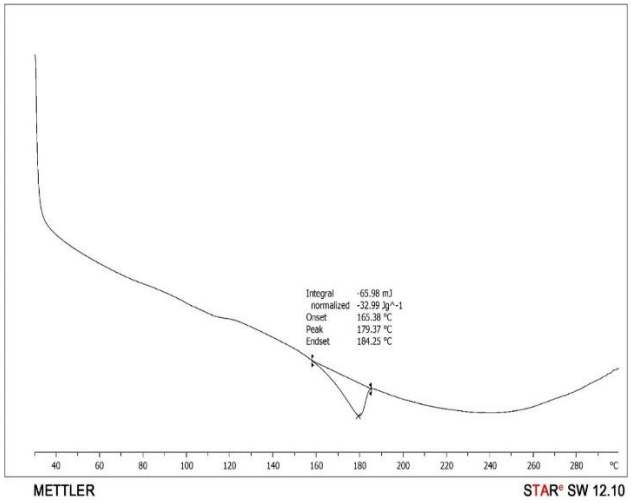

Figure 2: DSC Thermogram of Azelnidipine

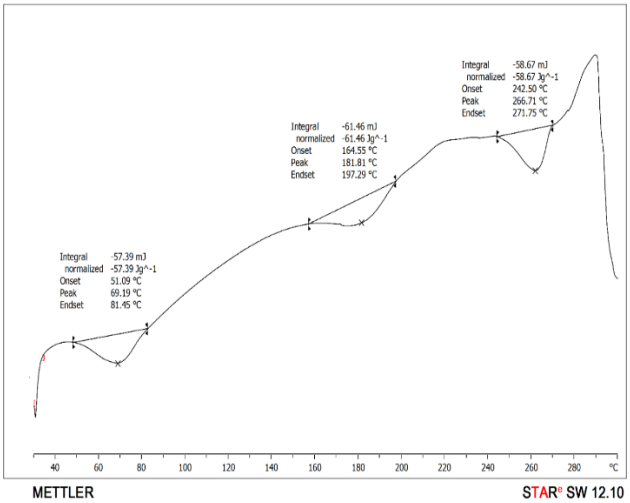

Figure 3: DSC Thermogram of Telmisartan with Eudragit RS100 and RL 100

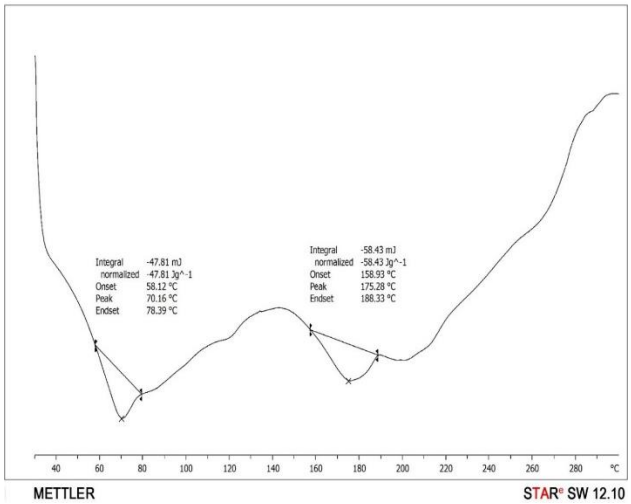

Figure 4: DSC Thermogram of Azelnidipine with Eudragit RS100 and RL 100

after each coating cycle was 3 min. Coating pan speed was used as 25 rpm. Coating of drug loaded pellets by polymeric solution was continued until reached to the desired weight gain of 5%, 10% and 15% w/w respectively. Finally, all coated pellets were store suitably at room temperature for further studies. Formulation of Coated pellets were given in (Table 2)[9-11].

Evaluation of Pellets

Fourier Transforms Infrared Spectroscopy

To verify that the medication in the formulations was chemically intact, the infrared (IR) spectra of the coated pellets and that of pure drug were compared. The samples were ground into a powder and combined with dry potassium bromide powder. The powdered combination was placed in a sampler and examined using a Jasco FTIR 4100 FTIR spectrophotometer.

Friability

Friability of pellets was determined by subjecting 10 g of pellets in (Roche friabilator) at 4 min at 25 rpm. The abraded samples were sieved and the pellets retained on the sieve were weighed and percent friability was calculated from the difference in the weight of the pellets before and after friability.

Flow Properties

Table 2: Formulation of Coated Pellets

Formulation Code	Weight Gain (%)	Drug loaded Pellets (g)	Eudragit RS 100: RL 100 (Ratio)	IPA (ml)	DCM (ml)	TEC (mg)	Talc (mg)
F1	5	50	80:20	70	30	0.75	0.25
F2		50	60:40	70	30	0.75	0.25
F3		50	40:60	70	30	0.75	0.25
F4		50	20:80	70	30	0.75	0.25
F5	10	50	80:20	70	30	0.75	0.25
F6		50	60:40	70	30	0.75	0.25
F7		50	40:60	70	30	0.75	0.25
F8		50	20:80	70	30	0.75	0.25
F9	15	50	80:20	70	30	0.75	0.25
F10		50	60:40	70	30	0.75	0.25
F11		50	40:60	70	30	0.75	0.25
F12		50	20:80	70	30	0.75	0.25

The flow properties of polymer coated pellets were studied by determining its Carr compressibility index and Hausner ratio. The data of the tapped density and bulk densities were utilized for the determination of flow properties of the coated pellets.

Drug Content

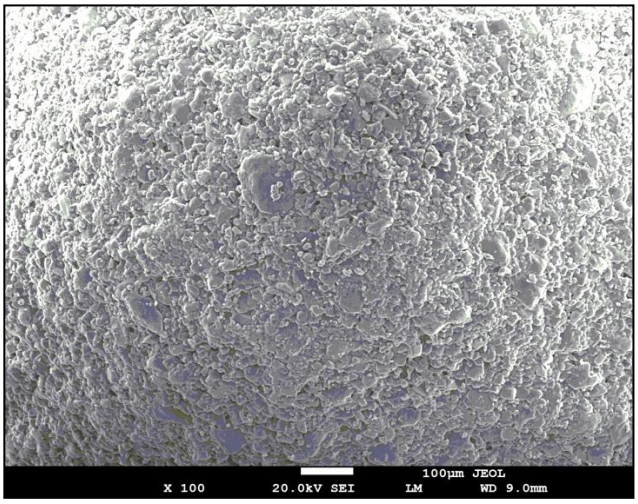

Figure 5: SEM of Uncoated Pellets

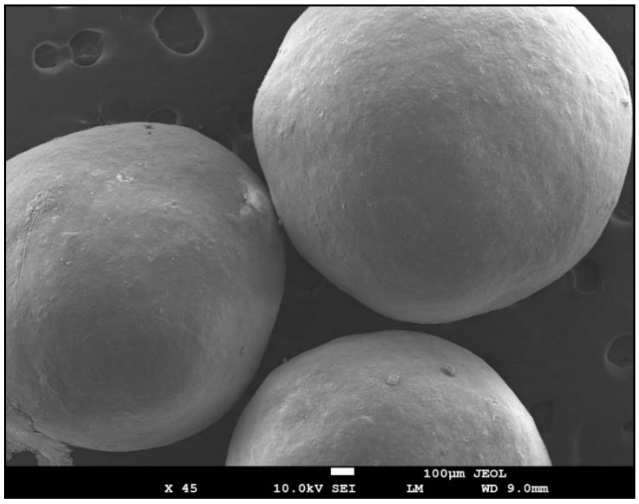

Figure 6: SEM of Coated Pellets a4 45 x

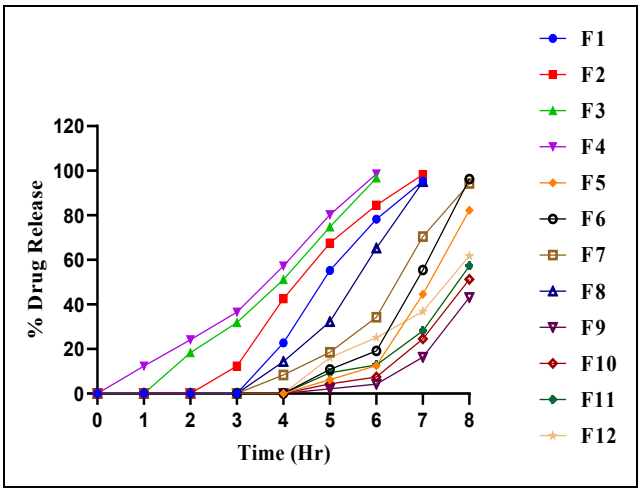

Figure 7: Dissolution profile of Telmisartan from Batch F1 to F12

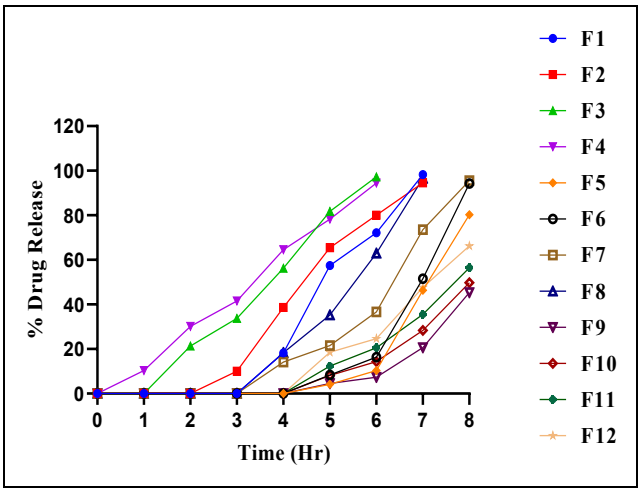

Figure 8: Dissolution profile of Azelnidipine from batch F1 to F12

Required weight of drug loaded pellets containing equivalent weight of telmisartan and azelnidipine were taken and crush to powdered. The powder was then transferred into 100 ml volumetric flask and dissolved in 100 ml of methanol. The solution was shaken and then filtered. After appropriate dilution the drug content was measured using a UV spectrophotometer by taking absorbance of sample at 255 nm.

Differential Scanning Calorimetry (DSC)

To assess any chance of interaction between drug, polymers, and other excipients was determined by DSC (Mettler, Germany). The DSC thermogram of the samples were obtained by placing the required amount of sample on sample holder pan and sample were heated over a temperature range of 0–350°C at a speed of 10°C/min under an inert atmosphere by using nitrogen gas as a purge gas at a rate of 50 ml/min.

Scanning Electron Microscopy (SEM)

Scanning electron microscopy was performed to examine the surface morphology of the formed pellets. SEM images of the pellets were taken before and after coating using (JEOL, Japan) Scanning microscopy. The sample was manually spread onto a sample stub with help of double adhesive carbon coated tape that was glued to an aluminum stub. Fine gold coating was applied with help of sputter coater under a pressure of 0.1 torr, that gives thin coating (30Å) of gold. The samples were examined at various magnification to examine surface morphology[12].

In-vitro Drug Release

A dissolution test instrument (Electrolab) was used for the *in vitro* drug release investigation. The investigation was carried out in 900 milliliters of dissolving media that was kept at 37±0.5°C using a basket. The basket rotated at 50 rpm. For the first two hours, polymer-coated pellets containing azelnidipine and telmisartan were added to 900 milliliters of 0.1N hydrochloric acid (pH 1.2) as a dissolution medium. For the remaining hours, the pellets were kept in phosphate buffer pH 6.8. Pipettes were used to remove 5 ml of samples at prearranged intervals. To maintain a constant total volume, the same volume of dissolving medium was promptly added back to the sample withdraw quantity. The sample was examined using a UV Spectrophotometer (Shimadzu 1700) at 296 nm and 255 nm for telmisartan and azelnidipine respectively after being diluted appropriately[13,14].

Stability Studies

Stability study on optimized formulation was conducted as per the ICH guidelines. Optimized formulation was sealed in a polyethylene pack and stored at 40 ± 2°C and 75 ± 5 % RH in the humidity chamber for 3 months. The samples were taken out of storage after required sampling time. The formulation was subjected to drug assay and *in vitro* dissolution studies. The value of similarity factor f2 was also calculated to compare the dissolution profiles before and after storage[15].

RESULTS AND DISCUSSION

Telmisartan and azelnidipine loaded pellets were prepared by using two grades of eudragit polymer (RS 100 and RL 100). Twelve different batches were prepared using fixed concentration (5%) of mixture of both polymers at different ratio. Polymer coating was done to achieve 5%, 10% and 15% weight gain of pellets. The effect of different weight gain of polymeric layer was assessed to its effect on lag time and drug release from coated pellets. Friability study of all batches of the coated pellets showed friability value less than 1% indicating mechanical strength of coated pellets.

Flow Properties

Tapped density and bulk densities for all the batches were falls within acceptable limit indicating good flow properties. Percent compressibility index and hausner ratio was calculated on the basis of bulk and tapped density, also indicates excellent flow properties for all batches of pellets. Compressibility index for all batches were found in the range of 10.59 ± 0.027 to 14.81 ± 0.030 %, while hausner ratio for all batches were found in the range of 1.11 ± 0.027 to 1.17 ± 0.026**.** Angle of repose value also confirmed the excellent flow properties for all batches, this may be due to spherical nature of pellets. The results are shown in (table 3).

Drug Content

Drug content for all batches coated pellets were determined after dissolving the pellets in methanol and after specific dilution. The sample were analysed spectrophotometrically for both the drug. The drug content values for all the batches were falls in the ideal range of pharmacopoeial standard indicates effective distribution and deposition of drug among the pellets. The results for drug content were shown in table 3.

Differential Scanning Calorimetry (DSC)

The DSC thermogram of Telmisartan (figure 1), showed a sharp endothermic peak at 269.85°C, (onset temperature at 267.87°C and endset temperature at 272.51°C) which confirmed the purity of the Telmisartan. Figure 2 represent the DSC thermogram of Azelnidipine showed the endothermic peak at 179.37°C (onset temperature at 165.38°C and endset temperature at 184.25°C) also confirmed the purity of Azelnidipine drug. Figures 3 and 4 represent DSC thermogram of drug telmisartan and azelnidipine with polymer eudragit RS 100 and RL 100 respectively. DSC thermogram of drug with polymer of both drug showed broadening of endothermic peak of drug along with little shift in melting peak temperature for both drugs, which confirmed that there is no any possible interaction between drug and polymer, indicates the both drugs are stable with polymers.

Scanning Electron Microscopy (SEM)

Scanning electron microscopy was performed to characterize the surface of the formed pellets. SEM photographs of the polymer coated nonpareil pellets were taken before and after coating using (JEOL, Japan) Scanning microscopy. Optimized formulation F6 was examined for its surface morphology by SEM. Surface morphology study showed smooth surface of coated pellets as compare to its uncoated pellets counterpart which showed rough surface. It was also observed that polymer coating on the pellets was uniform and free from cracks which can able to hold the drug for considerable time. The SEM image of uncoated and coated pellets were shown in figure 5, 6, 7 and 8 respectively.

Table 3: Characterization of formulations F1 to F12

Batch Code	Bulk density (g/cc)	Tapped density (g/cc)	Compressibility Index (%)	Hausner's Ratio	Angle of Repose(Ɵ)	Friability (%)	Tel Drug Content (%)	Azel Drug Content (%)
F1	0.288 ± 0.024	0.323 ± 0.014	10.83 ± 0.032	1.12 ± 0.024	20.32 ± 0.540	0.46 ± 0.24	97.32 ± 1.24	96.18 ± 2.18
F2	0.288 ± 0.014	0.328 ± 0.011	12.19 ± 0.026	1.13 ± 0.021	21.26 ± 0.602	0.42 ± 0.36	96.45 ± 0.87	98.60 ± 0.54
F3	0.284 ± 0.032	0.32 ± 0.017	11.25 ± 0.025	1.12 ± 0.031	20.5 ± 0.472	0.48 ± 0.12	98.41 ± 1.32	95.47 ± 1.22
F4	0.287 ± 0.016	0.336 ± 0.016	14.58 ± 0.031	1.17 ± 0.024	22.56 ± 0.543	0.51 ± 0.24	96.18 ± 1.58	96.48 ± 0.58
F5	0.28 ± 0.027	0.328 ± 0.024	14.63 ± 0.025	1.17 ± 0.026	24.64 ± 0.614	0.54 ± 0.18	99.14 ± 1.78	96.30 ± 1.23
F6	0.287 ± 0.018	0.321 ± 0.018	10.59 ± 0.027	1.11 ± 0.027	20.14 ± 0.862	0.42 ± 0.22	99.24 ± 1.74	98.18 ± 1.51
F7	0.278 ± 0.026	0.32 ± 0.015	13.12 ± 0.034	1.15 ± 0.032	21.34 ± 0.844	0.56 ± 0.31	97.36 ± 0.80	96.16 ± 0.62
F8	0.276 ± 0.012	0.324 ± 0.020	14.81 ± 0.030	1.17 ± 0.017	22.35 ± 0.723	0.44 ± 0.43	98.64 ± 1.65	95.14 ± 1.65
F9	0.283 ± 0.021	0.322 ± 0.026	12.11 ± 0.021	1.13 ± 0.020	24.36 ± 0.627	0.48 ± 0.12	96.87 ± 1.32	96.36 ± 1.14
F10	0.281 ± 0.014	0.319 ± 0.031	11.91 ± 0.018	1.13 ± 0.022	21.34 ± 0.581	0.52 ± 0.17	95.56 ± 0.85	99.12 ± 1.44
F11	0.282 ± 0.026	0.321 ± 0.014	12.14 ± 0.036	1.13 ± 0.032	24.18 ± 0.417	0.58 ± 0.26	98.47 ± 1.12	96.08 ± 0.85
F12	0.28 ± 0.012	0.324 ± 0.018	13.58 ± 0.041	1.15 ± 0.036	21.38 ± 0.926	0.50 ± 0.34	96.5 ± 1.47	98.17 ± 0.81

All values represent mean ± standard deviation (n=3)

Table 4: Kinetic Data Analysis of Formulations F1 to F12 for Telmisartan

Formulation Code	Zero Order	First Order	Higuchi	Korsmeyer-Peppas	
	R2	R2	R2	R2	'n'
F1	0.851*	0.71	0.621	0.773	0.492
F2	0.919*	0.733	0.714	0.896	0.269
F3	0.963*	0.729	0.778	0.932	0.225
F4	0.981	0.7	0.835	0.989*	1.05
F5	0.616	0.509	0.405	0.658*	0.544
F6	0.656	0.463	0.438	0.678*	0.572
F7	0.778	0.591	0.547	0.817*	0.498
F8	0.787*	0.592	0.549	0.78	0.491
F9	0.538	0.5	0.346	0.572*	0.431
F10	0.603	0.551	0.395	0.643*	0.471
F11	0.666	0.593	0.449	0.679*	0.493
F12	0.77*	0.697	0.539	0.685	0.524

*Indicates best fitted model

Table 5: Kinetic Data Analysis of Formulations F1 to F12 for Azelnidipine

Formulation Code	Zero Order	First Order	Higuchi	Korsmeyer-Peppas	
	R2	R2	R2	R2	'n'
F1	0.836*	0.724	0.526	0.715	0.465
F2	0.912*	0.808	0.638	0.882	0.304
F3	0.968*	0.765	0.796	0.917	0.251
F4	0.994*	0.852	0.882	0.989	1.04
F5	0.602	0.517	0.393	0.633*	0.542
F6	0.631	0.463	0.417	0.670*	0.565
F7	0.805	0.598	0.576	0.819*	0.478
F8	0.804*	0.7	0.522	0.718	0.435
F9	0.61	0.563	0.402	0.65*	0.454
F10	0.707*	0.553	0.481	0.682	0.487
F11	0.753*	0.693	0.521	0.686	0.513
F12	0.774*	0.707	0.542	0.685	0.54

*Indicates best fitted model

In Vitro Drug Release

In vitro drug release study of prepared coated pellets was determined by performing dissolution study in 900 ml of dissolution medium at 37±0.5°C using basket type apparatus at rotation speed of 50 rpm.

Drug loaded coated pellets formulation F1, F2, F3 and F4 was prepared with different ratio of Eudragit RS and RL 100 polymer, with weight gain of 5% showed 95.36%, 98.2%, 96.67% and 98.64% of telmisartan and 98.23%, 94.54%, 97.30% and 94.36% of azelnidipine release respectively, with lag time of 3 hrs, 2hrs, 1hrs and 0 hrs respectively. It was observed that differences in the permeability and porosity of Eudragit RS100 and RL 100 polymer majorly affect the lag time and drug release. It was observed that as the concentration of more permeable Eudragit RL 100 increases, the drug release rate also increased and lag time decreased, due to availability of more pore for diffusion of drug. From the study it was found that formulation batch F1 to F4 was not optimum in the maintaining lag time and drug release up to 8 hrs.

Formulation F5, F6, F7, and F8 prepared with similar composition of Eudragit RS and RL polymer with 10% of coating level weight gain, showed optimum drug release of 82.25%, 96.23%, 94.23% and 95.06% for telmisartan and 80.16%, 94.32%, 95.52% and 96.51% for azelnidipine at the end of 8 hrs. Batch F5 and F6 showed lag time of 4 hrs,

while batch F7 and F8 showed lag time of 3 hrs. This extended lag time in batch F5 and F6 might be due to higher concentration of less porous RS100, which provide minimum pathway for the drug release. Rate of drug release was slow up to the 6 hrs after that burst drug release was observed for both drugs. As the concentration of more porous RL 100 increased in batch F7 and F8, the fall in lag time and increased in drug release observed. Formulation batch F9 to F12 pellets was prepared with 15% of polymeric coating weight gain with similar polymeric composition like previous batches. *In vitro* dissolution study demonstrates the higher lag time and lower level of drug release. Retarded drug release for both the drug was observed in formulations, this might be because of high level of polymer coating which provide extended diffusion pathway for drug. Batch F9 to F12 meet the expectation of lag time but fails in drug release required for pulsatile drug delivery system.

From the above observation computed form dissolution data, it was concluded that coated pellets with 5% polymer load (F1 to F4) was not able to maintain sufficient lag time and, release the drug in faster rate and didn't meet the requirement for this type of formulation, while the coated pellets prepared with 15% polymer weight gain (F9 to F12) also not able to release sufficient amount of drug in 8 hrs, although it able to maintain the required lag time for drug release. Coated pellets prepared with 10% polymeric weight gain (F4 to F8) was considered to be effective in term of sufficient lag time and drug release in given time period. Thus this study clearly indicates that, 10% coating level with this polymeric ratio is more suitable in the formulation and development of pulsatile drug delivery of telmisrtan and azelnidipine. Among the all formulation, batch F6 prepared with eudragit RS100:Rl100 (60:40) ratio with 10% of polymeric level, was considered optimized on the basis of sufficient lag time and drug release for 8 hrs.

Kinetic Data Analysis

The kinetic data analysis was useful in determination of mechanism of drug release from the coated pellets. Obtained drug release rate profile of the prepared coated pellets formulations gave an idea about the drug release rate profile and the mechanism of the drug release. Drug release data of all batch formulation were determined and calculated for various kinetic models like zero order, first order, higuchi model and Korsmeyer-Peppas model for both drug. Fitting of the telmisartan release rate data to the various models revealed that formulations such as F1, F2 F3, F8 and F12 followed zero order release model, while F4, F5, F6, F7, F9, F10 and F11 followed Korsmeyer-Peppas release model. Optimized formulation F6 followed Korsmeyer-Peppas model. The 'n' value of Korsmeyer-Peppas model for formulation F6 was 0.572, which indicates that the drug release mechanism from coated pellets was non-Fickian diffusion. Similarly, Azelnidipine drug release rate was also fitted to various models, which showed that formulation F1, F2 F3, F4, F8, F10, F11 and F12 follows the zero order model, while formulation F5, F6, F7 and F9 follows Korsmeyer-Peppas model. Optimized formulation F6 followed Korsmeyer-Peppas model. The 'n' value of Korsmeyer-Peppas model for formulation F6 was 0.565, which indicates that the drug release mechanism from coated pellets was non-Fickian diffusion[16,17]. The details of Kinetic data analysis of formulations F1 to F12 for Telmisartan and Azelnidipine is shown in table 4 and 5.

Table 6: Stability Study on Optimized formulation (F6)

Drug	Results at 0 Month		Results at 3 Month	
	In-vitro Drug Release (%)	Drug content (%)	*In-vitro* Drug Release (%)	Drug content (%)
Telmisartan	96.23 ± 5.41	99.24 ± 1.74	97.18 ± 6.12	99.61 ± 1.02
Azelnidipine	94.32 ± 4.17	98.18 ± 1.51	96.42 ± 5.08	96.32 ± 1.12

Stability Study

In view of the potential utility of the formulation, stability studies were carried out on optimized formulation F6 at 45 °C and 75% RH for three months. The protocols of stability studies were in compliance with the guidelines in the WHO document for stability testing of products. After storage, the formulation was subjected to a drug assay and *in vitro* dissolution studies. The stability study showed no significant change after storage at 45 °C and 75% RH for three months There were no major changes in drug content and *in vitro* drug release in the formulation was observed. Similarity factor (f2) determined for before and after the stability period for both drug showed linearity in the drug release rate. F2 value for Telmisartan was found to be 73, while for those Azelnidipine it was found to be 75. F2 value clearly demonstrated that there was no major significant difference was observed in drug release pattern of optimized batch formulation when tested it for before and after stability. Stability study data suggested that the formulation is stable when kept at accelerated stability condition. Stability study data for optimized formulation, before and after the study periods was shown in (table 6).[18-31]

CONCLUSION

This study was aimed to develop the multiparticulate pulsatile drug delivery system containing telmisartan and azelnidipine. Drug loading pellets was developed by solution layring technique. drug loaded pellets was the coated with mixture of two grades of eudragit polymer RS 100 and RL 100. Coating was done to the extent of weight gain of pellets up to 5%, 10% and 15 %. Among the formulations multiparticulate pulsatile pellets developed with 10% weight gain showed optimum lag time of 4 hrs and delaying the drug release for 8 hrs. SEM study confirmed the effective and smooth coating of polymer over pellets surface. From the study it was colclude that, use of combination of polymer Eudragit RS 100 and RL 100, would be a better choice for the development of multiparticulate pulsatile drug delivery system.

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