International Journal of Applied Pharmaceutics

ISSN- 0975-7058 Vol 12, Issue 1, 2020

Original Article

SOLUBILITY AND DISSOLUTION RATE ENHANCEMENT OF TELMISARTAN BY SOLID DISPERSION AND PELLETIZATION TECHNIQUES USING SOLUPLUS AS CARRIER

VISWANADH KUNAM[1], DEVALA RAO GARIKAPATI[2], VIDYADHARA SURYADEVARA[3], VENKATA BASAVESWARA RAO MANDAVA[4], RAMESH BABU JANGA[5], SIVA PRASAD SUNKARA[6]

[1,3,5,6]Department of Pharmaceutics, Chebrolu Hanumaiah Institute of Pharmaceutical Sciences, Chandramoulipuram, Chowdavaram, Guntur 522019, Andhra Pradesh, India, [2]Department of Pharmaceutical Analysis, KVSR Siddhartha College of Pharmaceutical Sciences, Siddhartha Nagar, Vijayawada 520010, [4]Department of Pharmacy and Chemistry, Chairman, BOS, Chemistry and Pharmacy, Krishna University, Machilipatnam 521001, Krishna Dist., Andhra Pradesh, India
Email: viswanadhkunam9@gmail.com

Received: 06 Sep 2019, Revised and Accepted: 21 Oct 2019

ABSTRACT

Objective: In the present investigation, an attempt was made to improve the surface characters and solubility of the drug by solid dispersion and coating it on the nonpareil sugar beads as pellets.

Methods: Telmisartan solid dispersions were prepared by kneading method using soluplus. Crospovidone was added as disintegrant in pellets. Telmisartan pellets were prepared by dissolving soluplus and crospovidone in ethanol in different ratios and coated on nonpareil sugar beads as a drug layer by pan coating technique. Various physicochemical parameters like particle size, friability, angle of repose and drug content were evaluated for the prepared solid dispersions and pellet formulations. *In vitro* dissolution studies were carried out in pH 7.5 phosphate buffer using USP apparatus II. Fourier Transform Infrared Spectrometry, Differential Scanning Calorimetry and Scanning Electron Microscopic analysis were performed for solid dispersions, pellet formulations and its polymers to determine the interactions and surface characteristics.

Results: The physicochemical parameters were within the specified I. P limits. It was observed that the solid dispersion formulation TS_5 containing 1:5 ratio of telmisartan to soluplus showed better dissolution rate to the extent of 1.143 folds and 2.033 folds when compared to a marketed formulation and the pure drug, respectively. Similarly, pellet formulation TP_3 containing 1:3 ratio of telmisartan to soluplus showed an improved dissolution rate to the extent of 1.221 folds and 2.170 folds when compared to the marketed formulation and the pure drug, respectively. FTIR and DSC analysis revealed that there was no major interaction between the drug and the excipients.

Conclusion: From the present study, it was observed that the solubility of telmisartan was enhanced by soluplus in pellet formulations when compared to solid dispersions.

Keywords: Telmisartan, Soluplus, Crospovidone, HPMC E5, Solid dispersions, Pellets

DOI: http://dx.doi.org/10.22159/ijap.2020v12i1.35620. Journal homepage: https://innovareacademics.in/journals/index.php/ijap

INTRODUCTION

Multiparticulate oral drug delivery systems have acquired a centre stage in the arena of pharmaceutical research and development, thus provide greater opportunities in extending the first step of future pharmaceutical development. Multiparticulate drug delivery systems include pellets, granules, micro particles (like microspheres, microcapsules, and nanoparticles), mini tablets, mini depots, multiparticulate pulsatile drug delivery systems. Pelletized dosage forms date back to the 1950s, when the first product was introduced to the market. In 1949, research scientists of SmithKline and French developed tiny drug pellets that are filled into capsules. Since then, these dosage forms have gained considerable popularity because of their distinct advantages such as enhancement of drug dissolution; ease of coating with desirable release characteristics like sustained, controlled, delayed, site-specific or pulsatile delivery of drug from coated pellets; uniform packing; ease of capsule filling because of better flow properties due to its spherical shape; even distribution in the GI tract and less GI irritation. Pellets are obtained from diverse starting materials of fine powders or granules of bulk drugs and excipients utilizing different pelletization techniques [1]. Pellets intended for oral use are administered in the form of hard gelatin capsules or disintegrating tablets which quickly liberate their contents in the stomach and gets distributed throughout the gastrointestinal tract without loss of the depot effect and acts as self-contained depots [2, 3]. Pellets are prepared by different pelletization techniques like agitation by balling, compaction by compression and extrusion spheronization, layering and globulation by spray drying and spray congealing.

In the present experiment nonpareil sugar beads were coated with drug solution by layering technique. A well-controlled pelletization technique in which drug is layered onto starter seed materials which are coarse material or nonpareil, in powder, solution or suspension form with the aid of binder that assists heterogeneous pellets, consists of an inner core region and an outer shell region of a different composition [4, 5]. The nonpareil seeds must have spherical shape, smooth surface, uniform particle size distribution for uniform coating [6]. The concentration of the binder is based on the choice of the drug because it influences physical as well as mechanical properties of pellets and drug release from coated pellets. Commonly used binders include gelatin, povidone, carboxymethyl cellulose, hydroxyl propyl methyl cellulose, hydroxypropyl cellulose, sodium CMC, maltodextrins. Layering is classified into three categories: direct pelletizing, powder layering and solution or suspension layering [7, 8]. Materials suitable for use as starter cores in the production of coated pellets include sugar spheres consisting of saccharides and its derivatives like sugars, sucrose-starch mixtures, oligosaccharides and polysaccharides, microcrystalline cellulose spheres, pure drug crystals. Polymers which are plastic resins, inorganic substances like silica glass, hydroxyapatite and organic substances like activated carbon, acids like citric, fumaric, tartaric, ascorbic acids etc. can be employed [9].

Telmisartan was selected as a drug candidate for formulating drug coated pellets and solid dispersions for its improved dissolution characteristics. Telmisartan is an angiotensin II receptor blocker used for treatment of hypertension. This drug belongs to the BCS class II category and is highly insoluble in aqueous fluids. The absolute bioavailability of telmisartan is approximately 42-100%. After oral administration, the peak plasma concentration (Cmax) of telmisartan is reached after 1 to 2 h [10].

The main aim of present investigation was to formulate telmisartan solid dispersions and fast dissolving pellets by using nonpareil sugar beads as inert core material with soluplus as binder and solubility enhancer, crospovidone as disintegrant and ethanol was used as solvent to prepare the coating suspension to coat on the sugar beads as a drug layer by pan coating technique.

MATERIALS AND METHODS

Materials

Telmisartan was a gift sample from Pellets Pharma Ltd., Hyderabad. Soluplus, ethanol and HPMC E5 were procured from SD Fine Chem. Ltd., Mumbai. Crospovidone was a gift sample from M/S NATCO Pharma Ltd., Hyderabad.

Estimation of telmisartan

Validated UV Spectrophotometric method was used for the estimation of telmisartan. Telmisartan was estimated by measurement of absorbance at 296 nm in phosphate buffer of pH 7.5. The method was validated for linearity, accuracy, precision and interference. The method obeyed Beer's law in the range of 0–10 µg/ml concentration. Relative error and coefficient of variance were determined based on the results from repeatedly assayed samples. Standard drug solution was repeatedly assayed for 6 samples (n=6), and the relative error and coefficient of variance were found to be 0.72% and 1.5% respectively. There was no excipients interference observed [11, 12].

Methods

Preparation of solid dispersions by kneading method

Solid dispersions of telmisartan in different concentrations of soluplus were prepared by kneading method. The required quantities of drug and soluplus were dissolved in the solvent ethanol to get a clear solution in a dry mortar. The mixture was kneaded for 30 min by continuous trituration. Small volume of the solvent was added to maintain the mixture as thick slurry during kneading process. Trituration is continued until a dry mass was obtained. The mass obtained was further dried at 50 °C for 1 hour in a hot air oven. The dried product was powdered and passed through mesh no. 100 in each case. Various solid dispersions and their drug to carrier ratios are indicated in table 1 [13-15].

Table 1: Composition of telmisartan solid dispersions prepared by kneading method using soluplus

Formulation	Composition	Drug: Carrier ratio Telmisartan: Soluplus)
TS_1	Telmisartan: Soluplus	1:1
TS_2	Telmisartan: Soluplus	1:2
TS_3	Telmisartan: Soluplus	1:3
TS_4	Telmisartan: Soluplus	1:4
TS_5	Telmisartan: Soluplus	1:5

Preparation of pellets by pan coating method

A dispersion of crospovidone in purified water was prepared by using half of its quantity and it was initially applied on the sugar beads by using spray gun at a pan speed of 300 rpm while maintaining the temperature at 60 °C using IR lamp. The crospovidone coated beads were further dried at room temperature for 12 h. This coat acts as a base coat for applying the medicament on the beads. Coating solution was prepared by dissolving telmisartan, soluplus and remaining crospovidone in ethanol at different ratios. The crospovidone coated spheres then placed in a pan coater and coating solution was sprayed by using sprayer gun. Coating pan was operated at 300 rpm, while hot air is blown at 50 °C. Then these beads were further dried at room temperature for 12 h. The drug coated beads were finally coated with HPMC E5 dissolved in purified water by using spray gun at a pan speed of 300 rpm while maintaining the temperature at 50 °C using IR lamp. This coat acts as a protective layer and the finally coated beads were thoroughly dried in a tray drier at 60 °C for 1 hour. Then these beads were stored in a desiccator for further use [16, 17]. Various pellet formulations and their drug to carrier ratios are indicated in table 2.

Table 2: Composition of telmisartan pellet formulations prepared by pan coating method using soluplus

Formulation	Composition	Drug: carrier ratio telmisartan: soluplus)
TP_1	Telmisartan: Soluplus	1:1
TP_2	Telmisartan: Soluplus	1:2
TP_3	Telmisartan: Soluplus	1:3
TP_4	Telmisartan: Soluplus	1:4
TP_5	Telmisartan: Soluplus	1:5

Evaluation of physicochemical parameters on prepared granules

The physical parameters such as particle size, friability, angle of repose and drug content were evaluated for prepared formulations.

Particle size determination

The average particle size of the prepared solid dispersions and pellet formulations was analyzed by sieve analysis method [18].

Friability test

Roche friabilator was used to determine the friability. Pre-weighed pellets were placed in friabilator and rotated at a speed of 25 rpm for 4 min. The pellets were then re-weighed after removal of fine and the percentage of weight loss was calculated.

Angle of repose determination

Angle of repose was determined by passing the solid dispersions and pellet formulations through a funnel fixed to a burette stand at a particular height (4 cm). A graph paper was placed below the funnel on the table. The height and radius of pile were measured [19]. Angle of repose of the formulations was calculated using suitable formula.

$$Angle\ of\ repose\ (\theta) = \tan^{-1}\frac{h}{r}$$

Where h is height and r is the radius of the pile.

Drug content determination

Different formulations of telmisartan equivalent to 20 mg was weighed and transferred into a 100 ml volumetric flask. To this, small quantity of methanol was added to dissolve. It was shaken occasionally for about 15 min and the volume was made upto 100 ml by adding pH 7.5 phosphate buffer. The solution was filtered and the filtrate was subsequently diluted with pH 7.5 phosphate buffer and the absorbance was measured at 296 nm using pH 7.5 buffer as blank solution.

In vitro dissolution studies

The dissolution test for prepared solid dispersions and pellets was carried out in USP Apparatus Type II (paddle) with 900 ml of pH 7.5 phosphate buffer as dissolution medium. The temperature and rotations per minute (rpm) were maintained at 37±0.5 °C and 75, respectively. 5 ml samples were withdrawn at 5, 10, 15, 20, 30, 45 and 60 min. A fresh volume of the medium was replaced with same volume to maintain the sink conditions and the constant volume throughout the experiment. The samples withdrawn were suitably diluted with same dissolution medium and the amount of drug dissolved was estimated by ultraviolet spectrophotometer (UV 3000+) at 296 nm. The dissolution studies were carried out for 6 times on all the formulations.

Based on dissolution data, various dissolution parameters such as $T_{50}$and $DE_{30\%}$ first order constant and Hixon-Crowell constants were determined for various formulations. T_{50} is the time required for 50% of the drug to dissolve in suitable dissolution medium. It can be measured by plotting a graph taking time in minutes on X-axis and cumulative percent drug dissolved on Y-axis. The dissolution efficiency can have a range of values depending on the time intervals chosen. In any case, constant time intervals should be chosen for comparison. The index $DE_{30\%}$ would relate to the dissolution of drug from a particular formulation after 30 min and could only be compared with $DE_{30\%}$ of other formulations. It was calculated using the dissolved percentage curves of the drug versus time. Here, the region between the area above the curve and the total area of the graph were used for calculation and expressed in percentage.

Characterization of telmisartan formulations

Based on the dissolution studies, the optimized formulations were selected and FTIR and DSC studies were performed to know the drug and polymer interactions. SEM analysis was performed for pellet formulation and its polymers to know the surface characteristics.

Accelerated stability studies

The optimized formulations (TS_5 and TP_3) were subjected to accelerated stability studies as per ICH guidelines. They were kept in separate petri dishes after preparation and stored in thermo stated oven at a temperature and relative humidity (RH) of 25±2 °C, 60±5% RH for 6 mo and 40±2 °C, 75±5% RH for 3 mo. Then, they were evaluated for physical parameters, drug content and drug release studies.

RESULTS AND DISCUSSION

The compositions of various telmisartan formulations were given in table 3.

Table 3: Composition of telmisartan solid dispersions and pellet formulations

S. No.	Ingredients (mg/10 doses)	TS_1	TS_2	TS_3	TS_4	TS_5	TP_1	TP_2	TP_3	TP_4	TP_5
1.	Telmisartan	200	200	200	200	200	200	200	200	200	200
2.	Sugar Pellets	---	---	---	---	---	2000	2000	2000	2000	2000
3.	Soluplus	200	400	600	800	1000	200	400	600	800	1000
4.	Crospovidone	---	---	---	---	---	50	50	50	50	50
5.	HPMC E5	---	---	---	---	---	50	50	50	50	50
6.	Ethanol	q. s.	q. s.	q. s.	q. s.	q. s.	q. s.	q. s.	q. s.	q. s.	q. s.
7.	Purified Water	---	---	---	---	---	q. s.	q. s.	q. s.	q. s.	q. s.

mg = milligram; q. s = quantity sufficient

Evaluation of physicochemical parameters

All the solid dispersions were having the particle size of 250–260 µm, while the pellet formulations were found to have the particle size in the range of 840–845 µm. Friability loss for all pellet formulations were within the limits i.e.<0.8%. Angle of repose values indicated that all solid dispersion formulations were having good flow characteristics with angle of repose value ranging from 22–24 °, whereas pellet formulations were having excellent flow properties with angle of repose 16–18 °. Drug content was estimated for all formulations and found to be highly uniform in range of 18.20–19.78 mg/dose. Physicochemical parameters evaluated for telmisartan formulations indicated that all formulations were stable and possessing required limits as per literature. The values of physicochemical parameters of telmisartan formulations were given in table 4.

Table 4: Evaluation of physicochemical parameters of telmisartan formulations

S. No.	Formulation code	Particle size (µm) mean±SD	Friability (%W/W)	Angle of repose (°)	Drug content (mg/dose) mean±SD
1.	TS1	250±0.12	----	24	18.20±0.36
2.	TS2	255±0.39	----	22	19.08±0.19
3.	TS3	255±0.46	----	23	19.20±0.26
4.	TS4	260±0.36	----	22	19.17±0.43
5.	TS5	250±0.39	----	22	19.34±0.42
6.	TP1	840±0.27	0.2	18	19.38±0.12
7.	TP2	845±0.38	0.2	18	19.76±0.32
8.	TP3	840±0.29	0.1	16	19.78±0.22
9.	TP4	840±0.52	0.13	17	19.65±0.46
10.	TP5	845±0.46	0.12	17	19.64±0.12

n=3; µm=micrometer; %w/w= percentage weight by weight; SD= Standard deviation

In vitro dissolution studies

Dissolution profiles indicated that telmisartan pure drug released to the extent of 45.77% whereas the marketed formulation (TAZLOC-20) was released to the extent of 81.35% at one hour. Solid dispersions TS_1–TS_5 found to release the drug from 79.64 to 93.06% respectively. The prepared fast dissolving solid dispersions tend to increase drug release from 1.740 to 2.033 folds when compared to pure drug. Pellet formulationsTP_1-TP_5 was found to release the drug from 89.25–99.34%. These fast dissolving pellet formulations tend to increase the drug release from 1.949–2.170 folds when compared to pure drug and 1.097–1.221 folds when compared to the marketed formulation. It was observed that the dissolution rate of the solid dispersion formulation TS_5 showed better dissolution rate to the extent of 1.143 folds and

2.033 folds when compared to the marketed formulation and pure drug respectively. Similarly, formulation TP_3containing 1:3 ratio of telmisartan to soluplus the dissolution rate is increased to the extent of 1.221 folds when compared to marketed formulation and 2.170 when compared to pure drug. It was observed that the rate of dissolution is greatly increased with pellet formulations than compared to solid dispersions prepared. Formulation TP_3 pellets containing1:3 drug to polymer ratio exhibited better release characteristics when compared to formulation TS_5 containing 1:5 ratio of drug and polymer. This was due to increased surface area of the pellet formulations. Dissolution profiles were given in fig. 1 and 2. Past studies performed by several others also revealed that other than soluplus, polymers like PEG 6000, PVP K30, Eudragit L 100 can also be used to enhance the solubility of telmisartan [20, 21]. Other agents like Poloxamer 188, PVP K25 and sodium starch glycolate can also increase the dissolution rates of telmisartan [22, 23]. All these carriers enhance dissolution of poorly water soluble drugs depending upon the drug to carrier ratio.

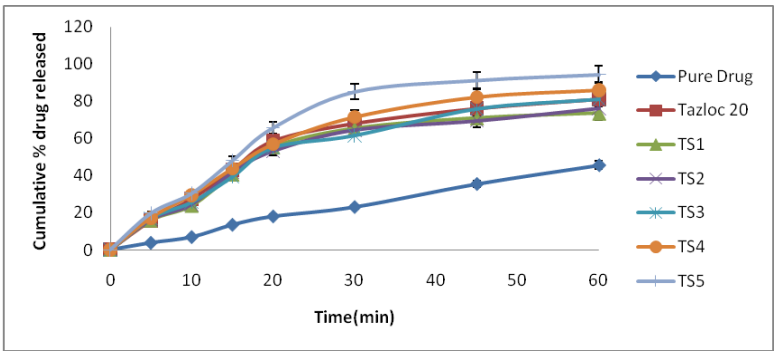

Fig. 1: Dissolution profiles of telmisartan fast dissolving solid dispersions (Results are expressed as mean±SD, n=3)

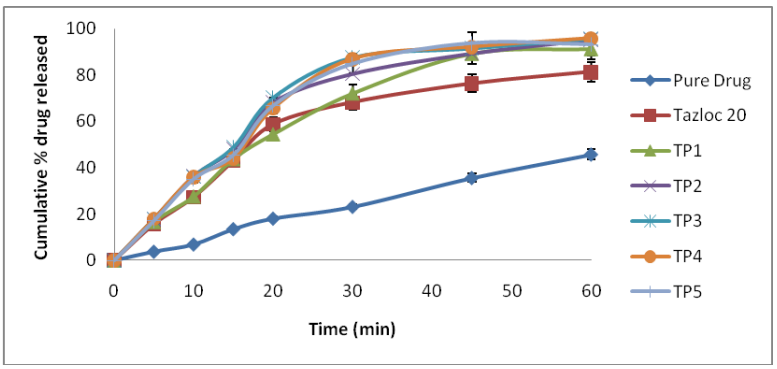

Fig. 2: Dissolution profiles of telmisartan fast dissolving pellets (Results are expressed as mean±SD, n=3)

Dissolution parameters such as T_{50} and DE_{30}% values were calculated for all the formulations. T_{50} for solid dispersions range from 9.75 to 19 min. Similarly, T_{50} for pellet formulation ranges from 9 to 17 min. DE_{30}% values for solid dispersions ranges from 38.3 to 60%. DE_{30}% values for pellet formulations ranges from 43.3 to 59.1%. Majority of the formulations displayed first order release kinetics and were found to be linear with R^2 values in the range of 0.926 to 0.994. The Hixon crowell constants for all the formulations were found to be linear with R^2 values ranging from 0.880 to 0.997 indicating that the drug release is by continuous depletion of the drug from the film formed across the spherical bead per unit weight. The results were indicated in table 5.

Table 5: *In vitro* dissolution kinetics of telmisartan formulations

S. No.	Formulations	T_{50} (min)	DE_{30} (%)	First order		Hixon crowell	
				R^2	K_1 (min^{-1})	R^2	K_{HC} ($mg^{1/3}$)
1	Pure drug	--	12	0.994	0.010	0.995	0.008
2	Marketed formulation (TAZLOC-20)	17.5	40	0.926	0.029	0.880	0.018
3	TS_1	19	38.3	0.972	0.025	0.968	0.015
4	TS_2	18	43.3	0.951	0.027	0.972	0.014
5	TS_3	14	46.6	0.965	0.029	0.971	0.016
6	TS_4	9.75	55.8	0.931	0.037	0.905	0.018
7	TS_5	9.75	60	0.940	0.043	0.903	0.021
8	TP_1	17	43.3	0.986	0.034	0.997	0.019
9	TP_2	9.5	53.3	0.985	0.045	0.971	0.022
10	TP_3	9	59.1	0.958	0.076	0.989	0.032
11	TP_4	10	56.6	0.981	0.064	0.991	0.029
12	TP_5	10	55.8	0.991	0.055	0.976	0.026

T_{50}= Time required for 50% of drug release; DE_{30}=Dissolution efficiency within 30 min; R^2= Regression coefficient; K_1= First order rate constant; K_{HC}= Hixon crowell rate constant

Characterization studies

FTIR analysis

The drug and excipient interactions were further characterized by IR Spectral analysis. FTIR Spectra of telmisartan pure drug, soluplus, optimised telmisartan solid dispersion and optimized telmisartan pellet formulation were obtained by KBr pelletization process. Spectra exhibited peaks, indicating the presence of-C-H Stretching and bending,-C=O Stretching, aromatic Para Substitution and–NH Wagging. Thus the FTIR Spectral analysis indicated that there were no drug interactions. The detailed spectra elucidations were shown in fig. 3, 4, 5 and 6 and indicated in table 6.

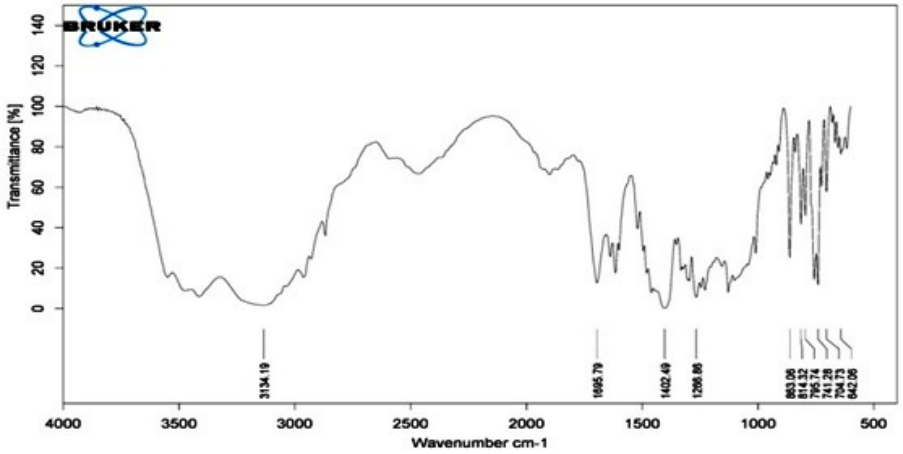

Fig. 3: FTIR interpretation of telmisartan

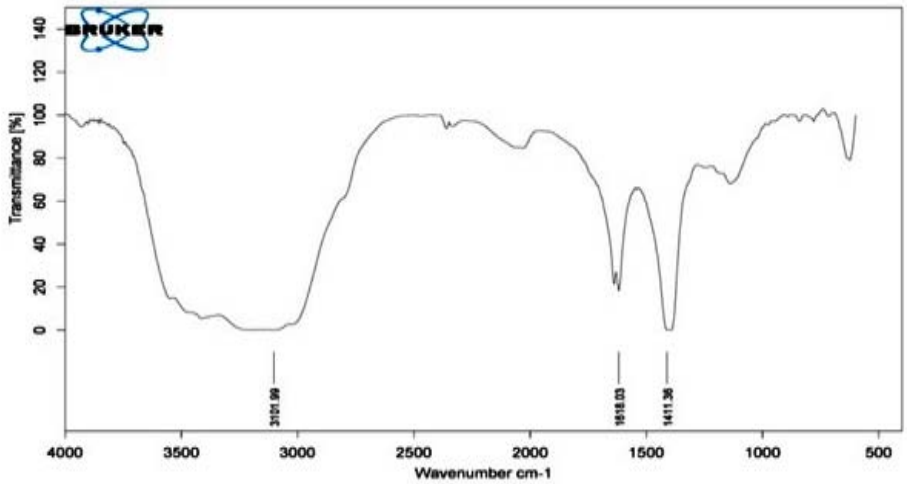

Fig. 4: FTIR interpretation of soluplus

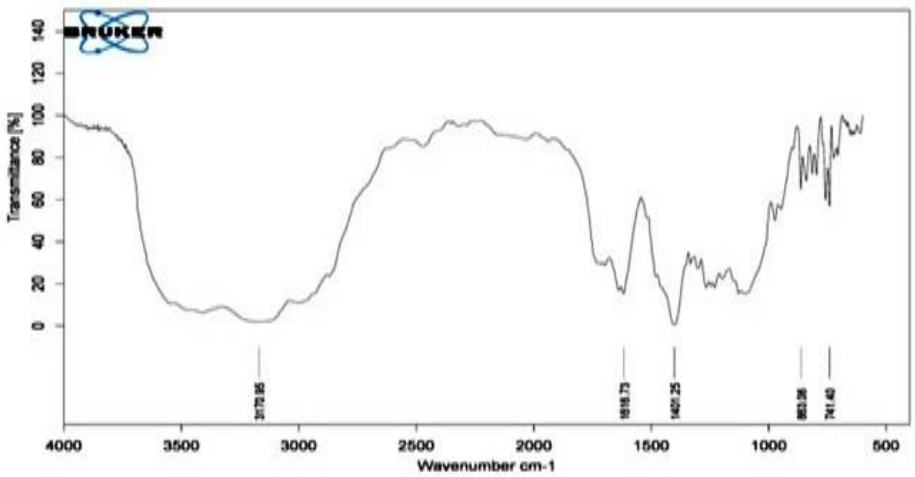

Fig. 5: FTIR spectra of optimized solid dispersion (TS5)

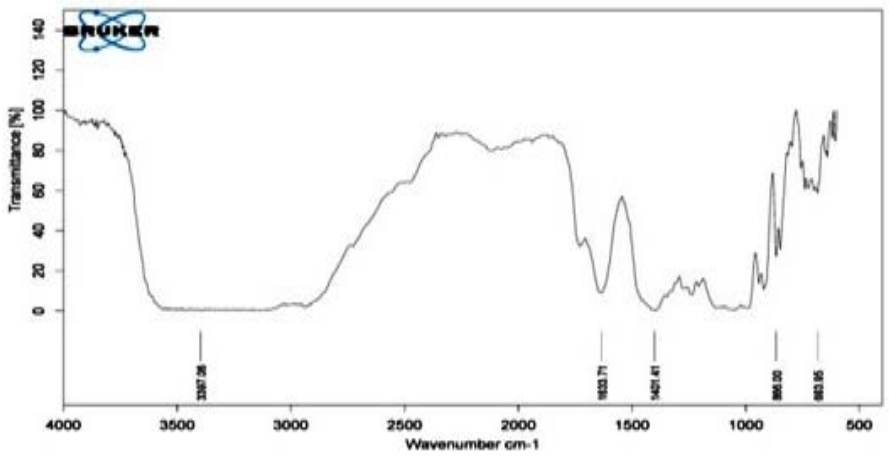

Fig. 6: FTIR spectra of optimized pellet formulation (TP3)

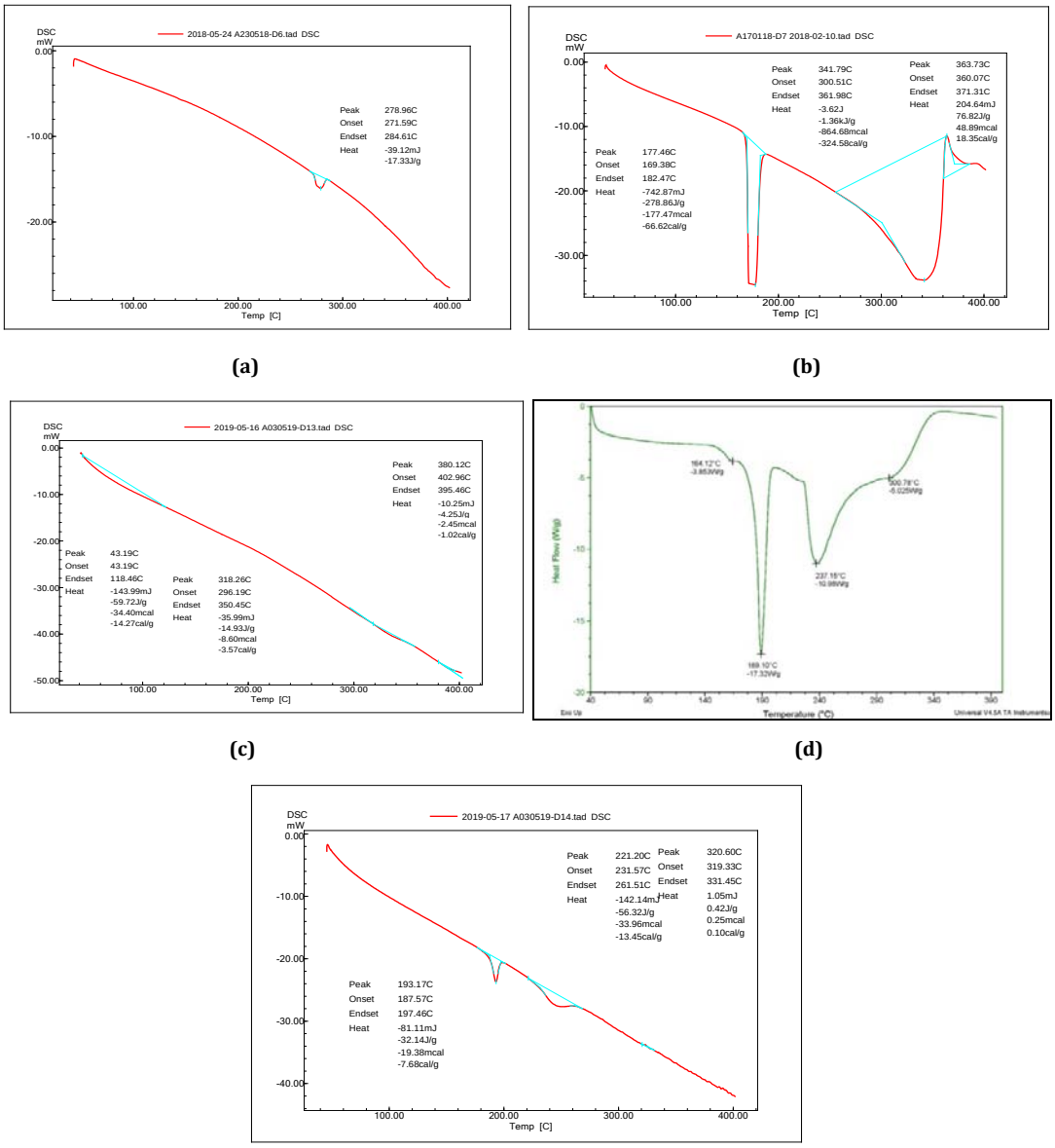

Fig. 7: DSC Images of (a) Telmisartan (b) Soluplus (c) Optimized Solid Dispersion (TS_5) (d) Pellets (e) Optimized Pellet Formulation (TP_3)

Table 6: FTIR spectrum interpretation for telmisartan formulations

Functional group	Wave number (cm^{-1})			
	Pure drug	Soluplus	TS5	TP3
C-H Stretching	3134.19	3197.51	3170.95	3397.06
C=O Stretching	1695.79	1617.59	1616.73	1633.72
C-H Bending	1402.49	1398.97	1401.25	1401.41
Para Substitution, aromatic	863.06	---	863.06	866.00
NH-Wagging	741.28	---	741.40	683.93

DSC thermograms

DSC thermograms indicated that the broad endothermic peak for telmisartan was observed at 278.96 °C, for soluplus, a narrow endothermic peak was observed at 177.46 °C, a broad endothermic peak at 341.79 °C and a sharp exothermic peak at 363.73 °C. The solid dispersions prepared by soluplus exhibited broad endothermic peaks at 318.26 °C and 380.12 °C. This indicated that the solid dispersions prepared were highly stable with molecular entrapment of telmisartan in soluplus. The sharp endothermic peak was observed at 189.10 °C and a broad peak at 237.15 °C for pellets. Similarly, a sharp endothermic peak at 193.17 °C, a broad endothermic peak at 221.20 °C and a small exothermic peak at 320.60 °C for soluplus was observed in the coated pellets indicated that the drug is molecularly entrapped in soluplus on the coated surface of sugar pellets. These studies indicated that there were no chemical interactions or decomposition between drug and polymers used in the formulations with the absence of additional peaks. The values were indicated in fig. 7.

Scanning electron microscopy (SEM)

The SEM analysis revealed the structure of telmisartan as crystalline and soluplus as spherical which were indicated in fig. 8. Solid dispersions prepared by kneading technique were found to be in fine amorphous form of dispersion where drug is totally entrapped into soluplus. The uncoated and coated sugar beads exhibited smooth surface with a uniform coating upon the coated pellets, thereby providing improved surface area for better dissolution rate.

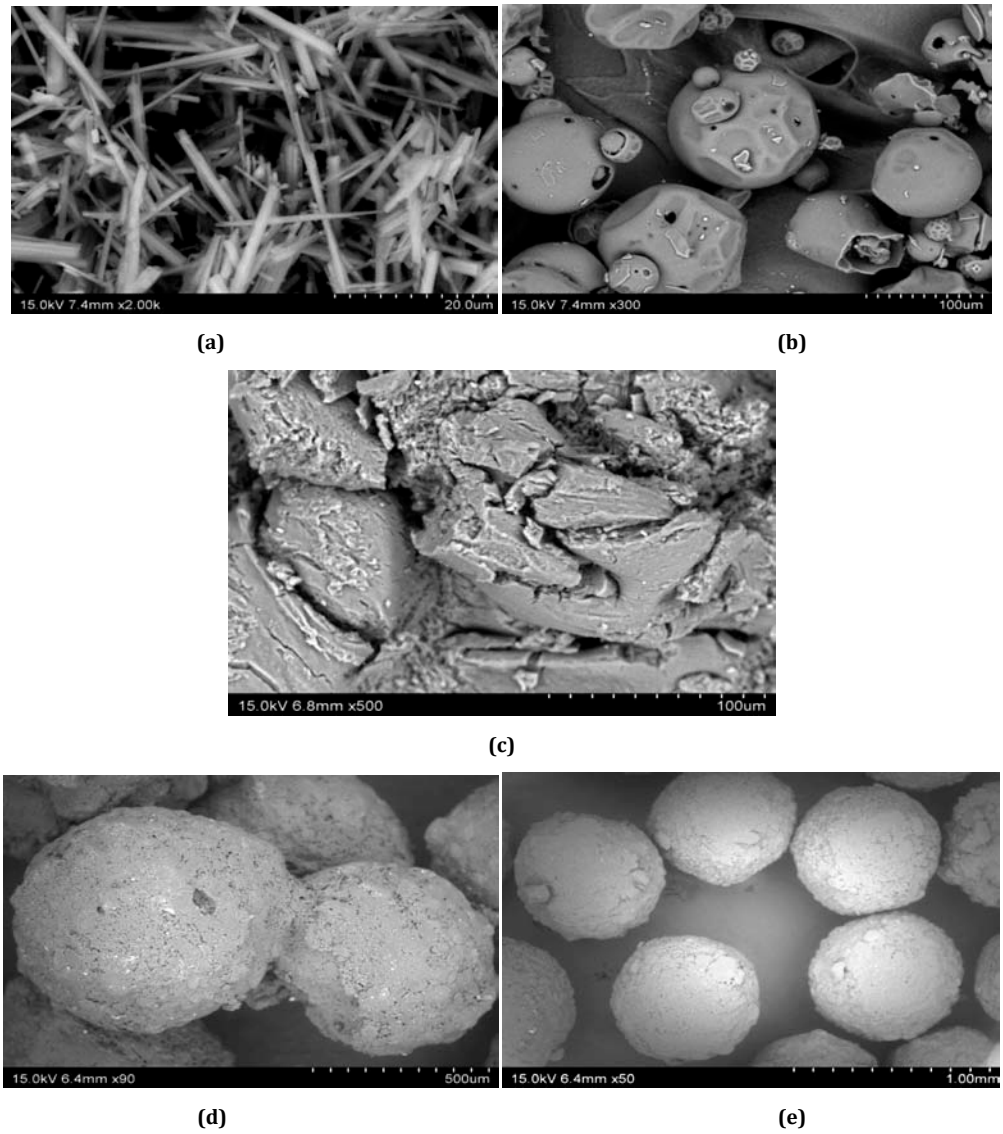

Fig. 8: Scanning electron microscopic images of (a) Telmisartan (b) Soluplus (c) Optimized Solid Dispersion (TS_5) (d) Pellets (e) Optimized Pellet Formulation (TP_3)

Accelerated stability studies

The optimized formulations TS_5 and TP_3 were subjected to accelerated stability studies as per ICH guidelines after storage at different conditions. Physical parameters and drug release studies were carried out on these formulations and the results were indicated in table 7 and fig. 9, 10 respectively.

Table 7: Parameters of formulations TS_5 and TP_3 under accelerated stability conditions

Formulation	Storage condition	Particle size (µm) mean±SD	Friability (% w/w)	Angle of repose (°)	Drug content (mg/dose) mean±SD
TS_5	Before Storage	250±0.39	----	22	19.34±0.42
	25±2 °C, 60±5% RH	250±0.31	----	22	19.29±0.22
	40±2 °C, 75±5% RH	250±0.29	----	23	19.27±0.39
TP_3	Before Storage	840±0.29	0.1	16	19.78±0.22
	25±2 °C, 60±5% RH	840±0.26	0.11	16	19.76±0.21
	40±2 °C, 75±5% RH	840±0.21	0.12	17	19.74±0.26

n=3; RH = Relative humidity; SD= Standard deviation

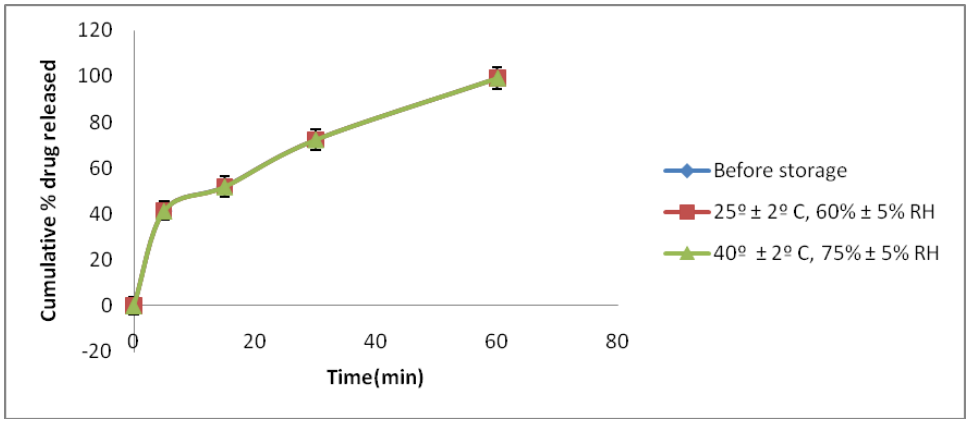

Fig. 9: Drug release studies of TS_5 before and after storage at different conditions (Results are expressed as mean±SD, n=3)

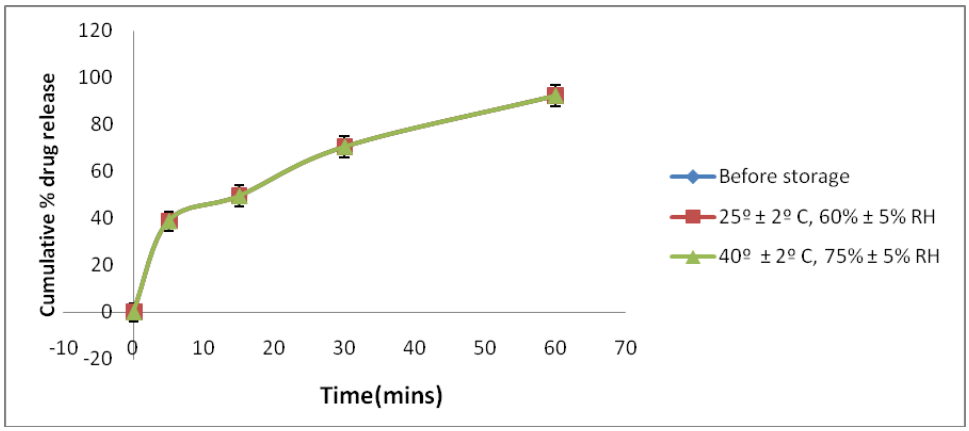

Fig. 10: Drug release studies of TP_3 before and after storage at different conditions (Results are expressed as mean±SD, n=3)

There was no significant change observed in physical parameters and drug release even stability studies at various storage conditions and indicated that these formulations were found to be stable.

CONCLUSION

Telmisartan solid dispersions and fast dissolving pellet formulations were prepared by using soluplus as a fast dissolving carrier. Among the various formulations prepared formulation $TS_5$and TP_3 prepared by solid dispersion technique and pelletization technique exhibited faster dissolution than compared to the marketed formulation and hence they are considered as optimized formulations. Hence it is concluded that pellet coating technique is found to be simple and stable when compared to other conventional solid dispersion techniques.

ACKNOWLEDGEMENT

The authors are thankful to Pellets Pharma Ltd., Hyderabad for a gift sample of telmisartan and management of Chebrolu Hanumaiah Institute of Pharmaceutical Sciences for providing the facilities to carry out the research work.

AUTHORS CONTRIBUTIONS

K. Viswanadh has performed the basic methodology of this work. S. Vidyadhara has guided the entire formulation and principle of the research work. G. Devala Rao has helped in the formulation studies. M. V. Basaveswara Rao and J. Ramesh Babu helped in the interpretation of FTIR and DSC data. S. Siva Prasad helped in the interpretation of SEM data.

CONFLICTS OF INTERESTS

The authors have no conflicts of interest

REFERENCES

1. Follonier N, Doelker E. Biopharmaceutical comparison of oral multiple-unit and single unit sustained release dosage forms. STP Pharma Sci 1992;2:141-55.
2. Vial Bernasconi AC, Doelker E, Buri P. Prolonged release capsules divided and monolithic forms. STP Pharma Sci 1988;4:397-409.
3. Malinowski HJ, Smith WE. Effect of spheronization process variables on selected tablet properties. J Pharma Sci 1974;63:285-8.
4. Jackson IM, Roberts S, Timmins P, Sen H. Comparison of laboratory scale processing in the production of coated pellets. Pharm Tech Int 1989;1:29-32.
5. Gamlen MJ. Pellet manufacture for controlled release. Manufacturing Chemist; 1985. p. 55-9.
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 PharmSciTech 2000;12:E9.
7. Olsen K. Fluid bed equipment. In: Ghebre Sellassie I. ed. Pharmaceutical Pelletization Technology. Marcel and Dekker, New York; 1989. p. 39-69.
8. Bauer KH, Lehmann K, Osterwald HP, Rothgang G. Equipment for sugar coating and film coating processes coated pharmaceutical dosage forms. Medpharm Scientiphic Publishers, Stuttgart; 1998.
9. Felton LA. Film coating of oral solid dosage form. In: Swarbrick J. ed. Encyclopedia of Pharmaceutical Technology. Informa Healthcare; 2007;3:1729–47.
10. Stangier J, Su CA, Roth W. Pharmacokinetics of orally and intravenously administered telmisartan in healthy young and elderly volunteers and in hypertensive patients. J Int Med Res 2000;28:149–67.
11. Tirumalesh N, Chowdary KPR. Formulation development and optimization of telmisartan tablets employing βcd starch 1500 and soluplus. Indo Am J Pharm Sci 2017;4:1630-5.
12. Vinit C, Rohini L, Jyoti S, Minal G, Supriya J. UV spectrophotometric method development and validation for telmisartan in bulk and tablet dosage form. Asian J Pharm Clin Res 2013;6:19-21.
13. Sucheta B, Dyandevi M, Mithun VK, Rajendra DP. Solubility enhancement of anti-hypertensive agent by solid dispersion technique. Int J Pharm Life Sci 2011;2:970–5.
14. Shankarguru P, Ramya Devi D, Vedha Hari BN. Effect of water content in kneading method of solid dispersion technique for solubility enhancement. Int J Appl Pharm 2017;9:14-21.
15. Poonam Arora, Jaspreet Singh, Renu Chadha. Physicochemical characterization and evaluation of telmisartan: hydroxypropyl-β-cyclodextrin: tween 80 inclusion complex. Int J Pharm Pharm Sci 2017;9:51-8.
16. Kausalya J, Suresh K, Padmapriya S, Anusha R, Senthilnathan B. Solubility and dissolution enhancement of telmisartan using various techniques. Int J Pharm Tech Res 2011;3:1737–49.
17. Ashwini K, Santosh S, Vivek R, Yogesh K, Ashish J. Review on antihyperlipidemic lipophilic drugs and their novel formulation approaches. Int J Pharm Pharm Sci 2017;99:1-8.
18. Gordon RE, Rosanske TW, Fonner DE, Anderson NR, Banker GS. Granulation technology and tablet characterization. Pharmaceutical dosage forms: tablets. 1990;2:324.
19. Train D. Some aspects of the property of angle of repose of powders. J Pharm Pharmacol 1958;10(S1).
20. Niranjan C, Anuradha C, Shubahngi S, Jagdish S. Improvement of bioavailability and solubility of telmisartan by solid dispersion technique using various carriers. Int J Pharm Sci Rev Res 2013;19:36–41.
21. Alatas FI, Ratih HE, Soewandhi SN. Enhancement of solubility and dissolution rate of telmisartan by telmisartan-oxalic acid cocrystal formation. Int J Pharm Pharm Sci 2015;7:423-6.
22. Jain AJ, Gohel DK, Patel KN, Patel BA, Patel PA. Use of combined techniques of solubilization for improving solubility and dissolution of immediate release tablet containing telmisartan. Int J Pharm Res Scholars 2012;1:221–31.
23. Venkatarao M, Vidyadhara S, Sandeep D. Formulation and evaluation of telmisartan solid dispersions using entada scandens seed starch and poloxamer-188 as superdisintegrants. Asian J Pharm Clin Res 2018;11:474-81.