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Original Article

SOLUBILITY AND DISSOLUTION RATE ENHANCEMENT OF TELMISARTAN BY SOLID DISPERSION AND PELLETIZATION TECHNIQUES USING KOLLIDON VA 64 AS CARRIER

K. VISWANADH[1*], G. VIJAYA KUMAR[2], M. V. BASAVESWARA RAO[3], S. VIDYADHARA[4]

[1]Krishna University, Machilipatnam, Andhra Pradesh, India 521004, [2]K. V. S. R. Siddhartha College of Pharmaceutical Sciences, Siddhartha Nagar, Vijayawada, Andhra Pradesh, India 520010, [3]Krishna University, Machilipatnam, Andhra Pradesh, India 521004, [4]Chebrolu Hanumaiah Institute of Pharmaceutical Sciences, Guntur, Andhra Pradesh, India 522019
Email: viswanadhkunam9@gmail.com

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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 solvent evaporation technique using Kollidon VA64 as binder and solubility enhancer, Crospovidone as disintegrant and ethanol was used as the solvent. Telmisartan pellets were prepared by dissolving telmisartan, kollidonVA64, Crospovidone in ethanol in different ratios and coated on nonpareil sugar beads as a drug layer by pan coating technique. All the formulations were further evaluated for physicochemical parameters such as particle size, friability, angle of repose and drug content. *In vitro* dissolution studies were carried out in pH 7.5 phosphate buffer by using USP apparatus II.

Results: It was observed that the dissolution rate of the solid dispersion formulation TSD_5 showed a better dissolution rate to the extent of 1.113 folds and 1.979 folds when compared to a marketed formulation and pure drug, respectively. Similarly, the formulation TPL_3containing 1:3 ratio of Telmisartan to Kollidon VA64 showed an improved dissolution rate to the extent of 1.150 folds and 2.045 folds when compared to the marketed formulation and pure drug, respectively. Majority of the formulations displayed first-order release kinetics and were found to be linear with R^2 values in the range of 0.905 to 0.994. FTIR analysis and DSC analysis revealed that there was no major interaction between the drug and the excipients used in the design of the formulation. SEM analysis was performed for solid dispersions, pellet formulations and its polymers to determine the surface characteristics.

Conclusion: From the present study, it was observed that the solubility of Telmisartan was enhanced by Kollidon VA 64 in pellet formulations when compared to solid dispersions.

Keywords: Telmisartan, KollidonVA64, Solid dispersions, Pellets

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INTRODUCTION

Multiparticulate oral drug delivery systems have acquired center 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, microparticles (like microspheres, microcapsules, nanoparticles), mini tablets, mini depots, multi particulate 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 the 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 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. Considering the final polymer solution to be sprayed, a normal HPMC-based system would have an appropriate viscosity. HPMC possess varying ratios of Hydroxypropyl and Methyl substitution, which in turns determine the organic solubility as well as thermal gelation temperature of aqueous solution. The extent of substitution is designated by the weight percentage of the substituent group attached to the ring; known as "degree of substitution" (D. S.). A lower D. S. results in lower solubility and is only soluble in a caustic solution. The letter "E", "K", "J" and "F" identify the different Hypromellose grade product with respect to their properties. The suffix "S" denotes "surface treated", "G" denotes "Granular grade" while "CR" denotes "Controlled Release" grade. In "E", "F" and "K" grade products, the substitution is major constituents, while in case of "J" it is about 50% of the total substitution [7]. A 5 mPa s grade is used (E5) a solids concentration of about 15%w/w can be achieved. This has the advantage over, for example, a coating solution prepared from a 50 mPa s grade (E50) where only a 5%w/w solids concentration could be achieved. The lower viscosity grade polymer permits a higher solid concentration to be used, with the consequent reduction in the solvent content of the solution. The practical advantage to be gained is that the lower the solvent content

of the solution, the shorter will be the processing time as less solvent has to be removed during the coating procedure.

Layering is classified into three categories: direct pelletizing, powder layering and solution or suspension layering [8, 9]. 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 [10].

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 the 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 [11].

The main aim of the present investigation was to formulate telmisartan solid dispersions and fast-dissolving pellets by using nonpareil sugar beads as inert core material with Kollidon VA64 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. Kollidon VA64, 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 [12].

Methods

Preparation of solid dispersions by solvent evaporation method

Solid dispersions of Telmisartan were prepared by mixing different ratios of telmisartan and KollidonVA64 and the mixture was allowed to dissolve in a suitable volume of ethanol. To this solution, Crospovidone was added and mixed for few minutes. Then the dispersions were evaporated by solvent evaporation technique at 40-50°C in a china dish using a heating mantle with constant stirring. The resultant solid dispersions were pulverized and then sieved through sieve no 60 to get the solid dispersion [13, 21, 22].

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 a 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, KollidonVA64 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 [14].

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 as per the standards.

Particle size determination

The average particle size of the prepared solid dispersions and pellet formulations was analyzed by the sieve analysis method [15].

Friability test

Roche friabilator was used to determine the friability. Pre-weighed pellets were placed in friabilator and rotated at a speed of 25rpm for 4 min. The pellets were then re-weighed after the removal of the 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 [16]. 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 up to 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 the 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 performedto 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 (TSD_5 and TPL_3) were subjected to accelerated stability studies as per ICH guidelines. They were kept in separate petridishes after preparation and stored in thermostated oven at a temperature and relative humidity (RH) of 25±2 ℃, 60±5% RH for 6 mo and 40±2 ℃, 75±5% RH for 3 mo. Then, they were evaluated for physical parameters, drug content and drug release studies.

RESULTS AND DISCUSSION

Telmisartan solid dispersions and fast dissolving pellets were prepared bysolvent evaporation and spray coating techniques respectively. Telmisartan along with Kollidon VA 64 were used at different ratios. While the drug and crospovidone concentration was maintained constantly. Nonpareil sugar beads were used as inert core material for pellet formulation. Ethanol was used as solvent to dissolve drug and other excipients. All the formulations were prepared under identical conditions to minimize processing variables. The composition of various telmisartan formulations were given in table 1.

Evaluation of physicochemical parameters

Telmisartan formulations prepared were further evaluated for physicochemical parameters such as particle size, friability, angle of repose and drug content estimation. All the solid dispersions were having the particle size of 250–260 µm, while thepellet 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 allsolid 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 2.

Table 1: Composition of telmisartan solid dispersions and pellet formulations

S. No.	Ingredients (mg/10 doses)	TSD_1	TSD_2	TSD_3	TSD_4	TSD_5	TPL_1	TPL_2	TPL_3	TPL_4	TPL_5
1.	Telmisartan	200	200	200	200	200	200	200	200	200	200
2.	Sugar Spheres	-	-	-	-	-	2000	2000	2000	2000	2000
3.	KollidonVA64	200	400	600	800	1000	200	400	600	800	1000
4.	Crospovidone	50	50	50	50	50	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.	q. s.	q. s.	q. s.	q. s.	q. s.

mg = milligram; qs = quantity sufficient

Table 2: 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.	TSD1	250±0.36	----	24	18.20±0.12
2.	TSD2	255±0.48	----	23	19.08±0.25
3.	TSD3	255±0.29	----	23	19.20±0.46
4.	TSD4	260±0.16	----	22	19.17±0.66
5.	TSD5	250±0.29	----	22	19.34±0.78
6.	TPL1	840±0.80	0.2	18	19.38±0.45
7.	TPL2	845±0.76	0.2	18	19.76±0.32
8.	TPL3	840±0.19	0.1	16	19.78±0.16
9.	TPL4	840±0.22	0.12	17	19.65±0.55
10.	TPL5	845±0.35	0.12	17	19.64±0.49

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

***In vitro* dissolution studies**

Dissolution studies were conducted for all the Telmisartan fast-dissolving formulations along with pure drug and the marketed formulation. Dissolution studies were performed by using USP apparatus type II (paddle type) with pH7.5phosphate buffer as medium, while maintaining bath temperature at 37±1 °C with a paddle operated at 75 rpm. 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 TSD_1–TSD_5 found to release the drug from 73.65 to 90.58%, respectively. The prepared fast-dissolving formulations tend to increase drug release from 1.609 to 1.979 folds than compared to pure drug and 1.059 to 1.113 folds when compared to the marketed formulation. Pellet formulationsTPL_1-TPL_5 was found to release the drug from 80.88–93.63%. These fast-dissolving pellet formulations tend to increase the drug release from 1.767–2.045 folds when compared to pure drug and 1.080–1.150 folds when compared to the marketed formulation. It was observed that the dissolution rate of the solid dispersion formulation TSD_5 showed better dissolution rate to the extent of 1.113 folds and 1.979 folds when compared to the marketed formulation and pure drug, respectively. Similarly, formulation TPL_3containing 1:3 ratio of telmisartan to Kollidon VA64 the dissolution rate is increased to the extent of 1.150 folds when compared to marketed formulation and 2.045 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 TPL_3 pellets containing 1:3 drug-to-polymer ratio exhibited better release characteristics when compared to formulation TSD_5 containing 1:5 ratio of drug and polymer. This was due to the increased surface area of the pellet formulations [17, 18]. Dissolution profiles were given in fig. 1 and 2. Past studies performed by several others also revealed that other than Kollidon VA64, polymers like PEG 6000, PVP K30, Eudragit L 100 can also be used to enhance the solubility of telmisartan [19]. Other agents like Poloxamer 188, PVP K25 and sodium starch glycolate can also increase the dissolution rates of telmisartan [20]. All these carriers enhance dissolution of poorly water soluble drugs depending upon the drug to carrier ratio.

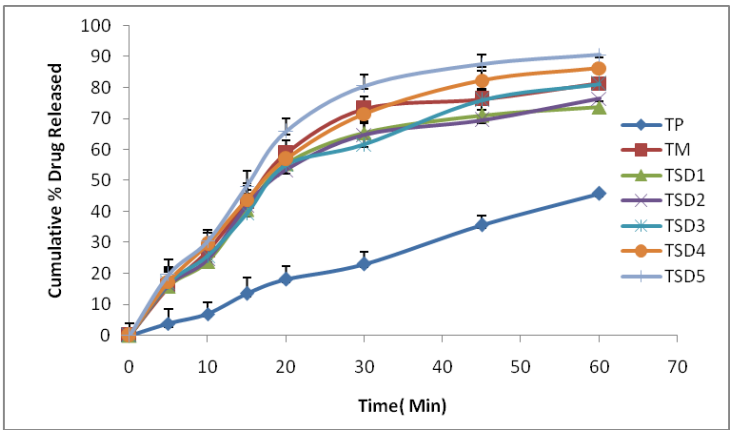


Fig. 1: Dissolution profiles of telmisartan fast dissolving solid dispersions (Results are expressed as mean±SD, n=3)

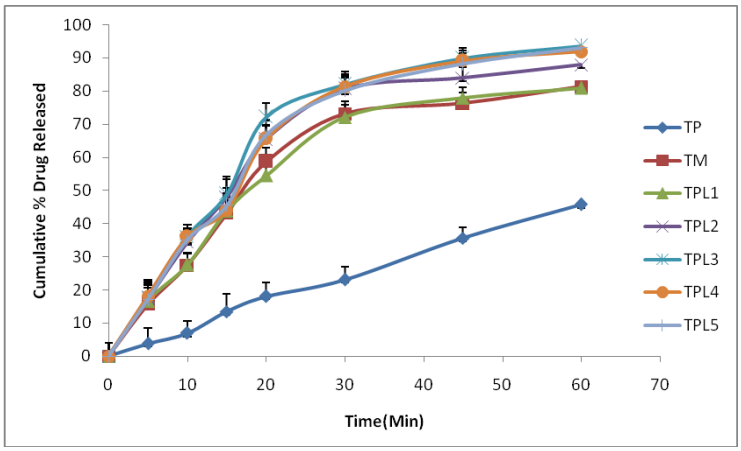


Fig. 2: Dissolution profiles of telmisartan fast dissolving pellets (Results are expressed as mean±SD, n=3)

Dissolution parameters such as $T_{50}$and DE_{30}% values were calculated for all the formulations. $T_{50}$for solid dispersions ranges from 16 to 18.5 min. Similarly, T_{50} for pellet formulation ranges from 15 to 18 min. DE_{30}% values for solid dispersions ranges from 38.12 to 46.22%. DE_{30}% values for pellet formulations ranges from 40.31 to 48.90%. Majority of the formulations displayed first-order release kinetics and were found to be linear with R^2 values in the range of 0.905-0.994. The Hixon Crowell constants for all the formulations were found to be linear with R^2 values ranging from 0.859–0.995, 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 3.

Table 3: *In vitro* dissolution kinetics of telmisartan formulations

S. No.	Formulations	T_{50} (min)	DE_{30} (%)	Zero-order		First order		Hixon Crowell	
				R^2	K (mg/min)	R^2	K_1 (min^{-1})	R^2	K ($mg^{1/3}$)
1	TP (Telmisartan pure drug)		12.41	0.993	0.767	0.994	0.009	0.995	0.008
2	TM (Telmisartan marketed formulation)	17	41.23	0.825	1.332	0.926	0.027	0.882	0.018
3	TSD_1	18.5	38.12	0.817	1.206	0.905	0.023	0.859	0.015
4	TSD_2	18.5	37.88	0.843	1.221	0.942	0.023	0.906	0.015
5	TSD_3	18.5	37.68	0.885	1.662	0.978	0.027	0.953	0.018
6	TSD_4	17	41.24	0.871	1.413	0.978	0.034	0.949	0.021
7	TSD_5	16	46.22	0.830	1.486	0.961	0.041	0.915	0.024
8	TPL_1	18	40.31	0.843	1.331	0.939	0.027	0.900	0.018
9	TPL_2	17	46.13	0.807	1.425	0.933	0.036	0.880	0.022
10	TPL_3	15	48.90	0.813	1.520	0.973	0.046	0.922	0.026
11	TPL_4	16	46.32	0.839	1.512	0.969	0.043	0.926	0.025
12	TPL_5	16	46.35	0.842	1.521	0.984	0.046	0.943	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, the mixture of telmisartan and Kollidon VA64, telmisartan and sugar spheres, telmisartan solid dispersions were obtained by KBr pelletization process. Spectra exhibited peaks, indicating the presence of O-H,-C=C, =C-H and C=O, stretching and bending functional groups. 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 4.

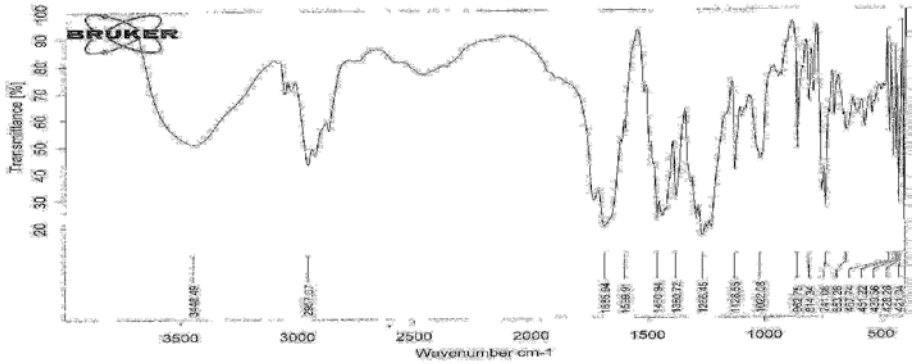


Fig. 3: FTIR interpretation of telmisartan

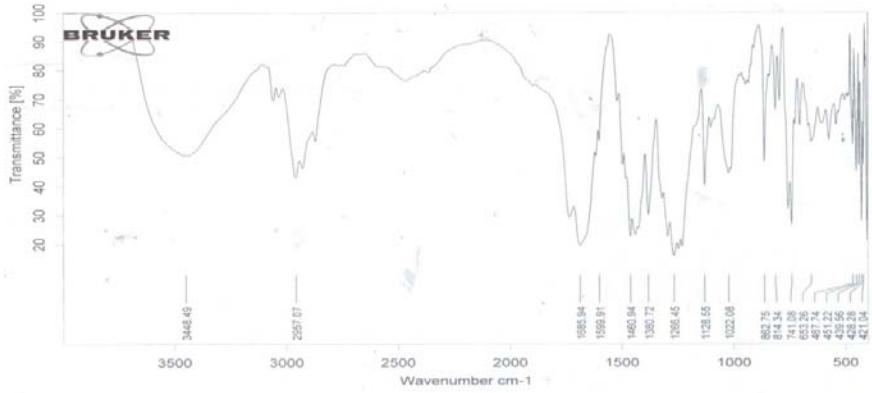


Fig. 4: FTIR interpretation of Kollidon VA64 and telmisartan

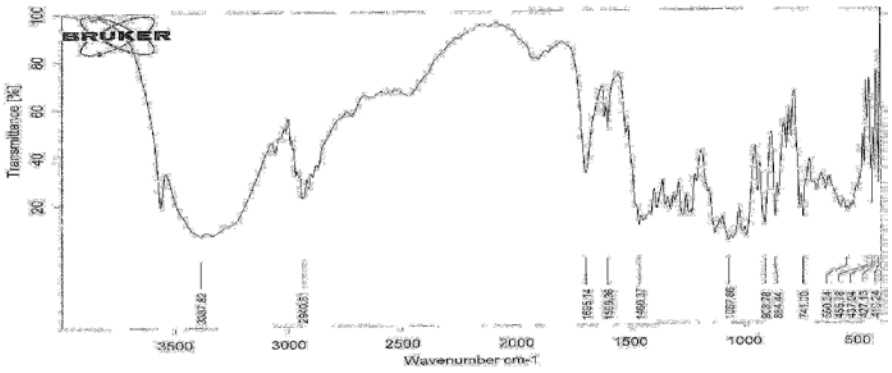


Fig. 5: FTIR interpretation of coated spheres (Spheres, kollidon and telmisartan)

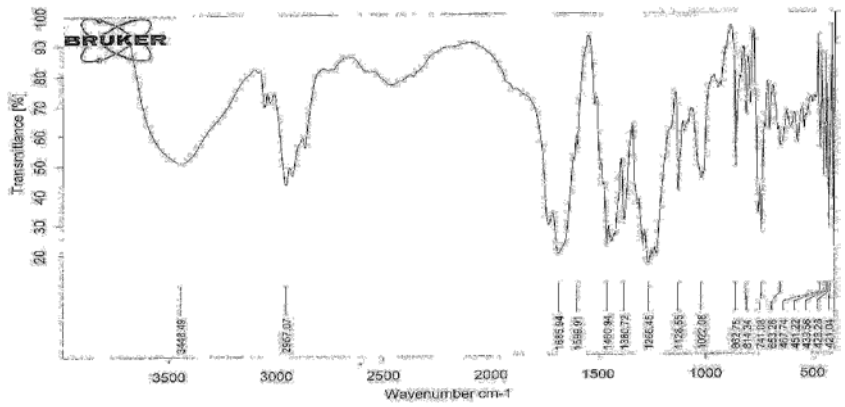


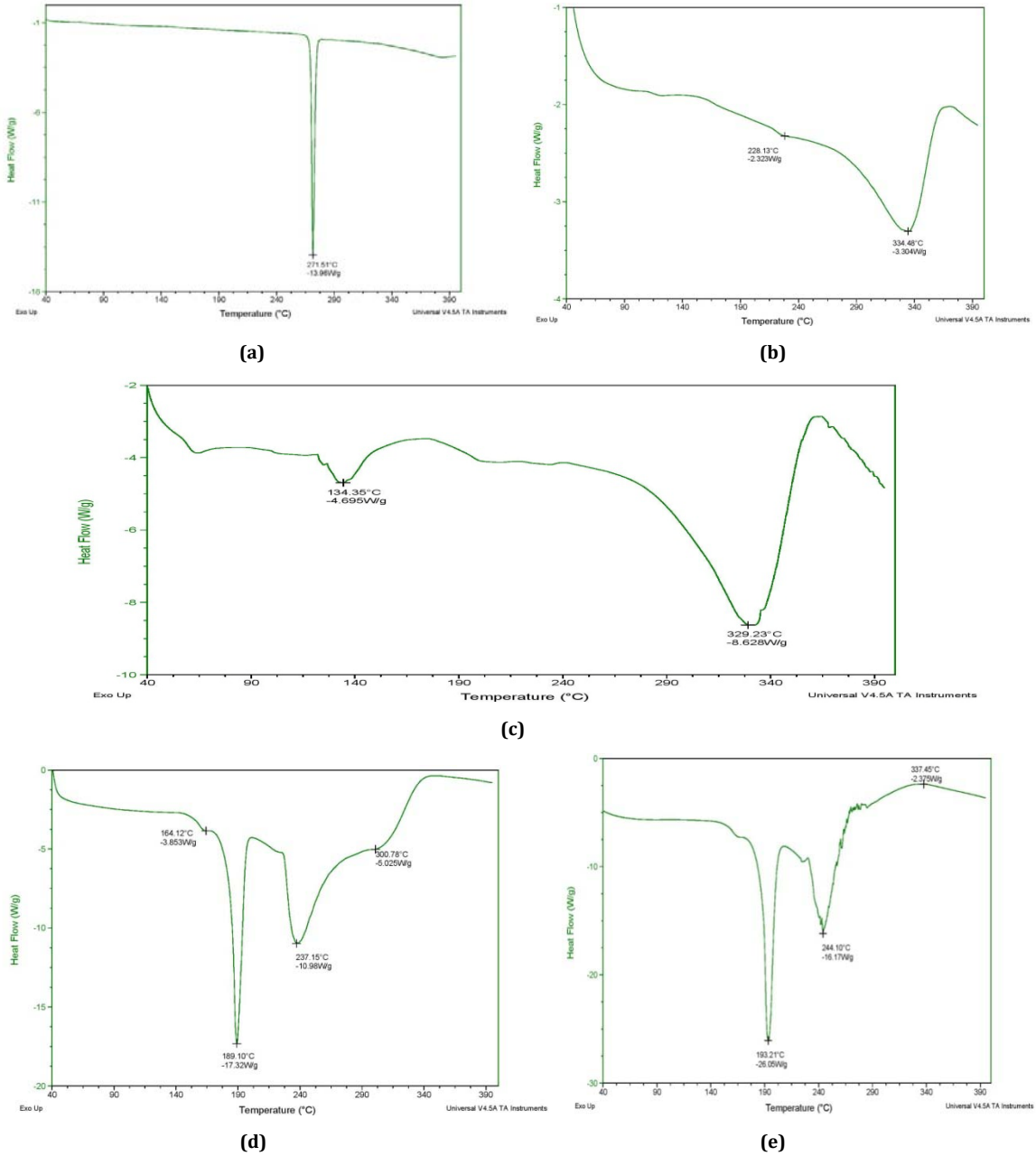
Fig. 6: FTIR interpretation of solid dispersions of telmisartan

Table 4: FT-infra red spectrum interpretation for telmisartan formulations

S. No.	Functional group	Telmisartan	Kollidon VA64+Telmisartan	Sugar spheres+Telmisartan	Solid dispersions+Telmisartan
1.	-OH (Carboxylic)	3402.18 cm^{-1}	3448.49 cm^{-1}	3387.82 cm^{-1}	3364.85 cm^{-1}
2.	C=C (Aromatic)	1696.79 $cm^{-1}$and 1459.92 cm^{-1}	1685.94 $cm^{-1}$and 1460.94 cm^{-1}	1695.14 cm^{-1} and 1460.37 cm^{-1}	1687.39 $cm^{-1}$and 1461.45 cm^{-1}
3.	=C-H (sp^2 Hybrid)	2958.35 cm^{-1}	2957.07 cm^{-1}	2940.61 cm^{-1}	2945.19 cm^{-1}
4.	-C=O(Carboxylic)	1696.79 cm^{-1}	1685.94 cm^{-1}	1695.14 cm^{-1}	1686.90 cm^{-1}

DSC thermograms

DSC thermograms indicated that the sharp endothermic peak for telmisartan was observed at 271.51 °C; for KollidonVA64, a broad endothermic peak was observed at 334.48 °C. The solid dispersions prepared by KollidonVA64 exhibited a broad endothermic peak at 329.23 °C and no further peaks were observed for the drug telmisartan. This indicated that the solid dispersions prepared were highly stable with molecular entrapment of telmisartan in KollidonVA64. The sharp endothermic peak was observed at 189.10 °C and a broad peak at 237.15 °C for sugar spheres. Similarly, a sharp peak at 193.21 °C, a broad peak at 244.10 °C and a small broad peak at 337.45 °C for KollidonVA64 was observed in the coated spheres, indicated that the drug is molecularly entrapped in KollidonVA64 on the coated surface of sugar spheres. These studies indicated that there were no chemical interactions or decomposition between the drug and polymers used in the formulations, with the absence of additional peaks. The values were indicated in fig. 7.



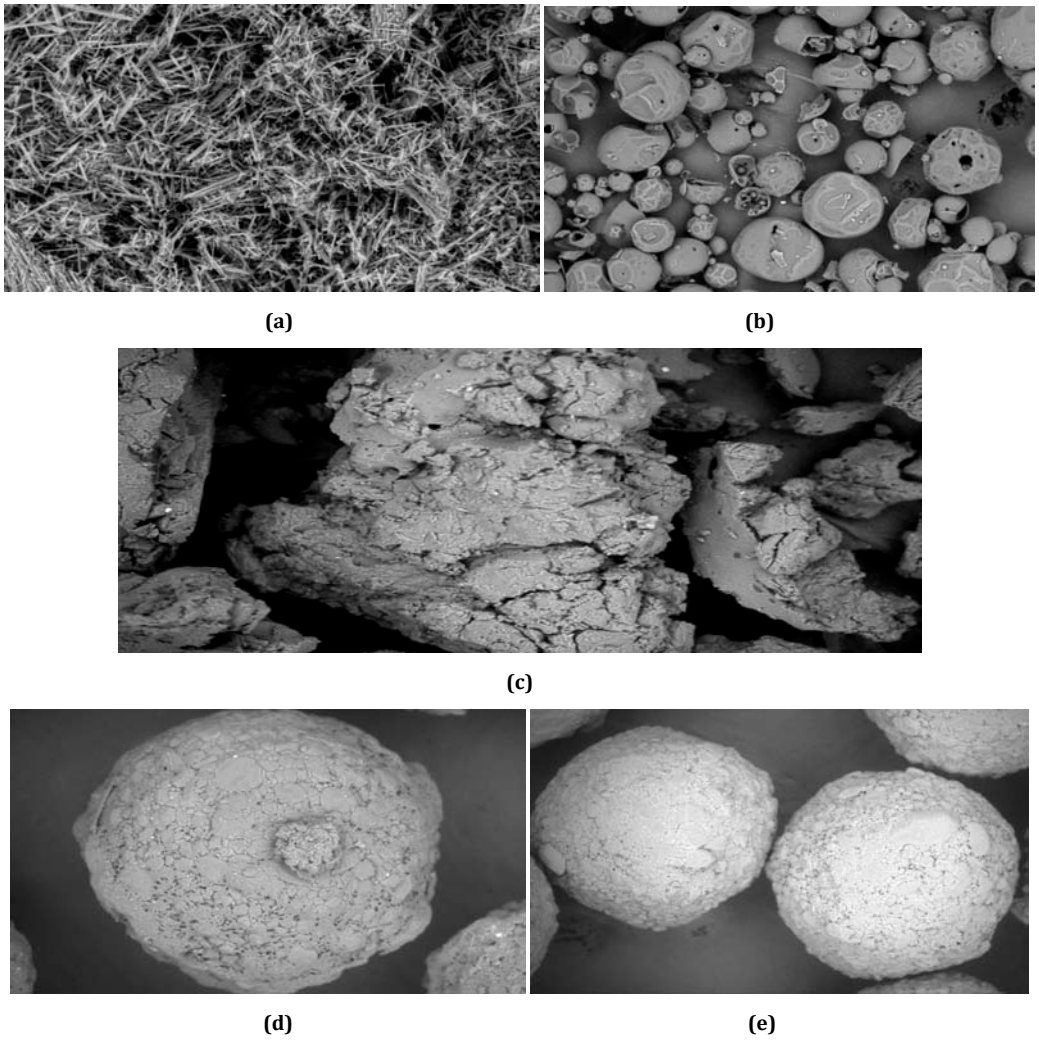
(a) **(b)** **(c)** **(d)** **(e)**

Fig. 7: DSC images of (a) Telmisartan (b) Kollidon VA64 (c) Solid dispersion (d) Sugar spheres (e) Coated spheres

SEM analysis

The SEM analysis revealed the structure of telmisartan as crystalline and KollidonVA64 as spherical, which was indicated in fig. 8. Solid dispersions prepared by solvent evaporation technique were found to be in a fine amorphous form of dispersion where drug is totally entrapped into KollidonVA64. The uncoated and coated sugar beads exhibited a smooth surface with a uniform coating upon the coated pellets, thereby providing improved surface area for a better dissolution rate.

Scanning electron microscopy (SEM)



(a) **(b)**

(c)

(d) **(e)**

Fig. 8: SEM images (500x) of (a) Telmisartan (b) Kollidon VA64 (c) Solid Dispersions (d) Sugar Spheres (e) Coated spheres

Table 5: Parameters of formulations TSD_5 and TPL_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
TSD_5	Before Storage	840±0.18	----	22	19.34±0.45
	25±2 °C, 60±5% RH	840±0.32	----	22	19.32±0.31
	40±2 °C, 75±5% RH	840±0.48	----	23	19.31±0.48
TPL_3	Before Storage	250±0.29	0.10	20	19.78±0.11
	25±2 °C, 60±5% RH	250±0.75	0.10	20	19.76±0.62
	40±2 °C, 75±5% RH	250±0.68	0.11	21	19.75±0.54

RH = Relative humidity; SD= Standard Deviation

Accelerated stability studies

The optimized formulations TSD_5 and TPL_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 5.

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

CONCLUSION

From the literature survey, it was evident that Solid dispersion formulations were found to enhance the dissolution rate of Telmisartan. Hence in this study, a combination of both Solid dispersion and pellet formulations of Telmisartan were prepared with an intention to study the dissolution profile of pellet formulations in comparison to solid

dispersions. Telmisartan solid dispersions and fast-dissolving pellet formulations were prepared by using kollidonVA64 as a fast-dissolving carrier. Among the various formulations prepared, formulations TSD_5 and TPL_3 prepared by pelletization technique and solid dispersion technique exhibited faster dissolution than compared to the marketed formulation and hence they are considered as optimized formulations. Hence it is concluded that the pellet coating technique is found to be simple, stable and economical when compared to other conventional solid dispersion techniques.

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AUTHORS CONTRIBUTIONS

All the authors have contributed equally.

CONFLICT OF INTERESTS

Declared none

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