Acta Scientific Pharmaceutical Sciences

Volume 2 Issue 1 January 2018

Research Article

Dissolution Improvement of Telmisartan by Surface Solid Dispersion Method

A Supriya*, B Manasa, TN Shilpa, Rajesh Kaza, S Savithramma and D Prasadu

Department of Pharmaceutics, Jawaharlal Nehru Technological University Anantapur, India

***Corresponding Author:** A Supriya, Department of Pharmaceutics, Sri Padmavathi School of Pharmacy, Jawaharlal Nehru Technological University Anantapur, India.

Received: December 30, 2017; **Published:** January 11, 2018

Abstract

The present study was aimed to improve the aqueous solubility and bioavailability of telmisartan by Surface solid dispersion technique. Surface Solid dispersions of Telmisartan were prepared by using hydrophilic polymers such as Avicel PH101, Alginic acid and Aerosil200. In different weight ratios by solvent evaporation method. The drug and the solid dispersions were characterized by saturation solubility studies, *in-vitro* dissolution, Fourier-transform infrared spectroscopy, drug content estimation. The hydrophilic polymers, such as Avicel PH101, Alginic acid, and Aerosil200 were found to be effective in increasing the aqueous solubility and dissolution rate of Telmisartan in surface solid dispersions when compared to the pure drug.

Keywords: Telmisartan; Bioavailability; Aerosil; Solid Dispersion *In Vitro* Drug Release

Abbreviations

SSD: Surface Solid Dispersion; BCS: Biopharmaceutical Classification System; FT-IR: Fourier Transform Infrared Spectra

Introduction

Solubility has a crucial role in the success of a drug development. Compounds with low solubility not only cause problems for *in vitro* and *in vivo* assays, but also add significant burden to drug development. Drug discovery and drug development often have different solubility screening requirements and methodologies have been developed to meet the needs of these different stages. The solubility behavior of drugs remains one of the most challenging aspects in formulation development [1].

Bioavailability of poorly water-soluble hydrophobic drugs is limited by their solubility and dissolution rate.

Several studies were carried out to increase the dissolution rate of drug [1]. One such study was solid dispersion which has shown promising results in improving solubility, wettability, dissolution rate of drug and subsequently its bioavailability. The mechanism by which solid dispersion enhances the solubility and dissolution involves particle size reduction to fine form or molecular level, conversion of crystalline form to amorphous form and by enhancing wettability [2,3].

It is defined as technique for dispersing one or more active ingredients on water insoluble carrier of extremely high surface area to achieve increased bioavailability and dissolution rates of insoluble drugs. Surface solid dispersion uses the solvent deposition technique to increase the solubility, dissolution and bioavailability of many insoluble or poorly water soluble drugs. *In-vivo* results have improves the release profile of many drugs resulting in rapid onset of bioavailability [4].

The solvent deposition technique involves deposition of the drug on the surface of the carrier by using volatile solvents. Deposition of the drug leads to reduction in its particle size, thereby providing a faster dissolution rate. Surface modifications is SSD formulations using hydrophilic carriers can alter the dissolution behaviour of hydrophilic carriers can alter the dissolution behaviour of hydrophobic drug materials [5].

The carriers used in the surface solid dispersions are water insoluble, porous materials which are hydrophilic in nature. The common tablet excipients like avicel, cab-O-sil, and crospovidone have been used as carriers for SSD. Drug release from the carrier material depends on the hydrophilic nature, particle size, porosity and surface area of the carrier. The larger the surface area of the carrier available for adsorption of drug, the better the release rate. Selection of carrier and method of preparation are the critical factors influencing the properties of drug incorporated in the SSD [6].

Surface solid dispersion technique has been extensively used to increase the solubility, dissolution and bioavailability of many practically insoluble or poorly water soluble drugs such as piroxicam, meloxicam, ibuprofen and ketoprofen [7].

Advantages of Solid Dispersions

- Reduction in particle size.
- Improved wettability.
- Improved porosity of drug.
- To decrease the crystalline structure of drug in to amorphous form.
- To improve solubility of a poorly water-soluble drug.
- To mask the taste of the drug substance.
- To prepare rapid disintegration oral tablets.
- To obtain a homogenous distribution of small amount of drugs at solid state.

- To stabilize unstable drugs.
- To formulate a faster release priming dose in a sustained release dosage form.
- They can be used as an alternate to parenteral therapy for immediate action.
- Solid dispersions improve the onset of action for drugs such as NSAIDs where immediate action is crucial in relieving acute pain and inflammation.
- Bioavailability of anticancer drugs has been improved by incorporating them in solid dispersions.

Disadvantages of Solid Dispersions

- Reproducibility of its physicochemical properties.
- Physical and chemical stability of drugs and vehicles.
- The scale up of manufacturing processes.

Materials and Methods

Preparation of standard curve of Telmisartan

5 mg of Telmisartan was accurately weighed and transferred in to 50 ml standard flask and then volume was made up of 50 ml with methanol. Pipette out 0.2 ml, 0.4 ml, 0.6 ml, 0.8 ml and 1 ml from above solution transferred in to the 10 ml standard flask and diluted to 10 ml with phosphate buffer of PH 7.4. Absorbance of the prepared solutions was determined spectro photometrically at 296 nm. The experiment was repeated for six times. Phosphate buffer of PH 7.4 was used as blank. A graph was plotted with concentration of Telmisartan (mcg/ml) on X-axis against absorbance (nm) on Y-axis [8].

Surface Sold Dispersion Technique

In the present study, surface solid dispersion of Telmisartan were prepared by solvent evaporation method.

Solvent evaporation method

Surface solid dispersion of Telmisartan with a hydrophilic carrier were prepared in different ratios of drug carrier. The solvent evaporation method was used for the preparation of surface solid dispersion in the present studies. In this method, 0.5g of Telmisartan was accurately weighed and dissolved in a minimum amount of methanol in which hydrophilic carrier was suspended. The solvent was evaporated by using a water bath at 45°C.The obtained solid was ground, sieved through a sieve no. 60 and store it in an air tight container [9].

S. No.	Ingredients	F1	F2	F3
1.	Telmisartan	0.5	0.5	0.5
2.	Avicel PH101	0.5	1	1.5
3.	Alginic acid	0.5	1	1.5
4.	Aerosil200	0.5	1	1.5
5.	Solvent volume (ml)	10	10	10

Table 1: Composition of Different Formulations of surface solid dispersion.

Characterization of Surface Solid Dispersion

FT-IR Spectroscopy

Fourier transform infrared (FT-IR) spectral measurements for Telmisartan AvicelPH101, Alginic acid, and Aerosil200 and their surface solid dispersion (SSD's) were recorded using thermo-IR 200 FTIR spectrophotometer. Potassium bromide pellet method was employed. The pure drug and their SSD's formulation were finely ground with KBr to prepare the pellets under a hydraulic pressure of 600 psi and back ground spectrum was collected under identical conditions. Each spectrum was derived from 16 single average scans collected in the range of 4000 - 400 cm^{-1} at the spectral resolution of 2 cm^{-1} [10].

Evaluation of Telmisartan Solid Dispersion

Percentage Practical Yield

Percentage crystal yield was calculated to know about percent yield or efficiency of any method and thus its help in selection of appropriate method of formulation. The final weights of prepared solid dispersion were taken and percentage crystal yield was calculated with following equation [11].

% yield = Practical yield/Theoretical yield x 100

Drug Content

Equivalent weight of prepared micro crystals containing 10 mg of drug were taken and transfer into 100 ml standard flask and volume was made up of 200 ml with methanol. The resulting solution were filtered through a 0.45 micro membrane filter and suitably diluted. The absorbance of the solution was measure at 296 nm [12].

$$\text{drug content}(\%) = \frac{\text{experimentaldrugcontent}}{\text{theoreticaldrugcontent}} \times 100$$

In Vitro Dissolution Studies

In vitro dissolution studies of pure Telmisartan and solid dispersion were conducted with the USP type II apparatus. The dissolution studies were performed using phosphate of PH 7.4 buffer as dissolution medium at 37 + (or) -0.5 c. with 75 rpm speed. Samples of each preparation equivalent to 10 mg of drug were added in to the dissolution medium. The sample of 5 ml aliquots were withdrawn periodically (15, 30, 45 and 60 min) and filtered through 0.45 micro membrane filter. The withdrawn sample was replaced every time with same quantity of dissolution medium. The filtered solutions were diluted suitably. Samples were analyzed for their drug content by using UV spectrophotometer at wavelength of 296 nm. Percent of Telmisartan dissolved at various time intervals was calculated and plotted against time [13-15].

Results and Discussion

Standard curve of Telmisartan

In the present study, analytical method obeyed the beer- lamberts law in the concentration range of 2 - 10 mcg/ml and was

suitable for the estimation of Telmisartan using phosphate buffer pH 7.4. The value of or (correlation coefficient) for the linear regression equation was found to be more than 0.994 which indicates a positive correlation between the concentration of drug and the corresponding absorbance values.

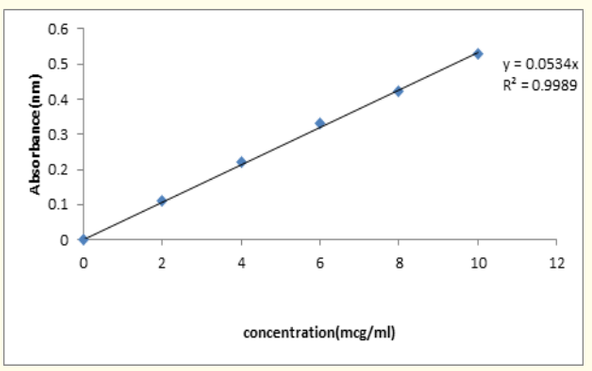

Figure 1: Standard curve of Telmisartan in phosphate buffer of Ph 7.4.

S. NO.	Concentration (in mcg/ml)	Absorbance
1.	2	0.131
2.	4	0.231
3.	6	0.332
4.	8	0.421
5.	10	0.530

Table 2: Standard curve data of Telmisartan using phosphate buffer pH 7.4.

FT-IR spectroscopy

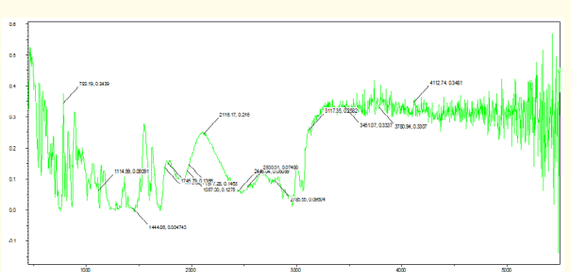

Figure 2: FT-IR spectroscopy of Telmisartan.

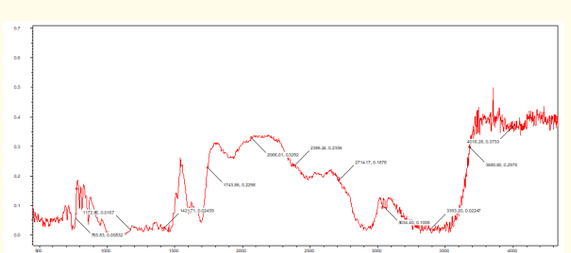

Figure 3: FT-IR spectroscopy of Avicel PH101.

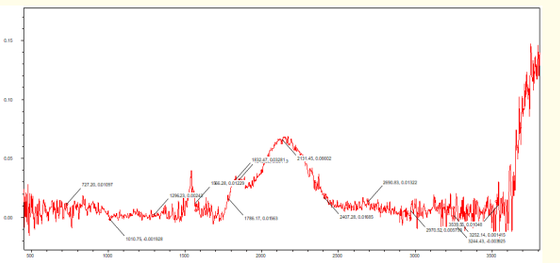

Figure 4: FT-IR spectroscopy of Alginic acid.

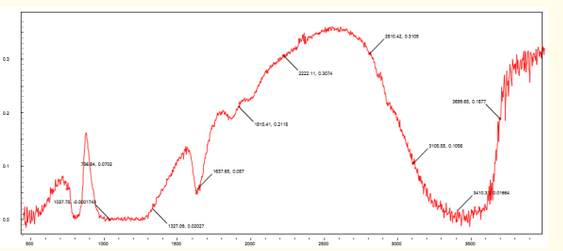

Figure 5: FT-IR spectroscopy of Aerosil200.

S. NO	Functional Group	Characteristic Peaks	Observed Peaks			
			Telmisartan	Alginic acid	Avicel PH 101	Aerosil200
1	C=C	1800 - 1600	1776	-	-	-
2	C=N		1977	-	-	-
3	C=O	1800 - 1600	1745	1786	1743	-
4	C-H	3500 - 3000	3117	3244	3680	3410
5	N-H	3500 - 3000	3451	-	-	-
6	C-C	1200 - 800	1114	1010	1172	-

Table 3: FT-IR Interpretation of pure drug and excipients.

Evaluation of Surface Solid Dispersion

Percentage practical yield

S. No.	Formulation code	% yield
1.	F1	93.4
2.	F2	96.0
3.	F3	99.5

Table 4: % practical yield of Telmisartan SSD containing Avicel pH101.

S. No.	Formulation code	% yield
1.	F4	84.0
2.	F5	86.8
3.	F6	91.6

Table 5: % practical yield of Telmisartan SSD containing Alginic acid.

S. No.	Formulation code	% yield
1.	F7	94.8
2.	F8	91.9
3.	F9	97.2

Table 6: % practical yield of Telmisartan SSD containing Aerosil200.

Percentage Drug content estimation

S. No.	Formulation code	% Drug content
1.	F1	87.73
2.	F2	90.94
3.	F3	91.69

Table 7: % Drug content of Telmisartan SSD containing Avicel pH101.

S. No.	Formulation code	% Drug content
1.	F4	66.79
2.	F5	74.90
3.	F6	89.62

Table 8: % Drug content of Telmisartan SSD containing Alginic acid.

S. No.	Formulation code	% Drug content
1.	F7	97.92
2.	F8	98.49
3.	F9	99.20

Table 9: % Drug content of Telmisartan SSD containing Aerosil200.

In Vitro Dissolution Studies

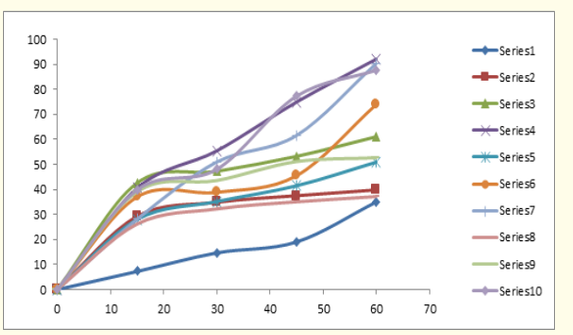

Figure 6: In vitro Dissolution profile pure drug and formulations.

S. No.	Time (min)	% Cumulative Drug Release									
		Pure Drug	F1	F2	F3	F4	F5	F6	F7	F8	F9
1.	15	7.26	29.04	42.45	40.45	27.92	36.98	28.01	26.03	38.86	39.81
2.	30	14.72	34.70	47.16	55.44	35.09	38.86	50.91	32.07	43.39	48.10
3.	45	19.08	37.29	53.11	74.94	41.35	45.47	61.50	34.91	50.94	77.35
4.	60	35.06	39.60	60.94	92.07	50.75	73.94	90.20	36.98	52.45	87.73

Table 10: Dissolution data of SSD's of Telmisartan.

Discussion

Telmisartan surface solid dispersions were prepared by solvent evaporation method using carriers like AvicelPH101, Alginic acid, Aerosil200. *In vitro* dissolution profiles of Telmisartan surface solid dispersions were compared with that of the pure telmisartan. All the formulations viz. F1-F9 has shown increased cumulative dissolution profiles are shown in table 10 and figure 6.

In addition, employing solvent evaporation technique in the preparation of Telmisartan surface solid dispersions would have reduced the particle size of the drug; there by facilitating faster dissolution rate, this may be due to deposition of the drug on the surface of an inert carrier.

In case of Telmisartan SSDs prepared with AvicelPH101 viz. formulations F1-F3 have shown increased cumulative dissolution profiles when compared to that of pure Telmisartan. The increased dissolution profiles observed for Telmisartan SSDs containing aerosil200 at regular time intervals were shown in table 10 and figure 6. From the results, it was found that the percentage drug release of pure Telmisartan was very low and only % was dissolved within 60 minutes. F1 formulation containing Telmisartan and Avicel PH101 in 1:1 ratio shows the release of 39.60 at the end of 1 hour. F2 formulation containing Telmisartan and Avicel PH101 in 1:2 ratio shows the release of 60.94% at the end of 1 hour. F3 formulation containing Telmisartan and Avicel PH101 in 1:3 ratio shows the release of 92.07% at the end of 1 hour.

In case of Telmisartan SSDs prepared with Alginic acid viz. formulations F4-F6 have shown increased cumulative dissolution profiles when compared to that of pure Telmisartan. The increased dissolution profiles observed for Telmisartan SSDs containing Alginic acid at regular time intervals were shown in table 10 and figure 4. From the results, it was found that the percentage drug release of pure Telmisartan was very low and only % was dissolved within 60 minutes. F4 formulation containing Telmisartan and Alginic acid in 1:1 ratio shows the release of 50.75% at the end of 1 hour. F5 formulation containing Telmisartan and Alginic acid in 1:2 ratio shows the release of 73.94% at the end of 1 hour. F6 formulation containing Telmisartan and Alginic acid in 1:3 ra-

tio shows the release of 90.20% at the end of 1 hour.

In case of Telmisartan SSDs prepared with Aerosil200 viz. formulations F7-F8 have shown increased cumulative dissolution profiles when compared to that of pure Telmisartan. This could be due to reduction in particle size of drug, deposition of drug on the surface of the inert carrier and improved wettability. The increased dissolution profiles observed for Telmisartan SSDs containing Aerosil200 at regular time intervals were shown in table 10 and figure 5. From the results, it was found that the percentage drug release of pure Telmisartan was very low and only % was dissolved within 60 minutes. F7 formulation containing Telmisartan and Aeosil200 in 1:1 ratio shows the release of 36.98% at the end of 1 hour. F8 formulation containing Telmisartan and Aerosil200 in 1:2 ratio shows the release of 52.45% at the end of 1 hour. F9 formulation containing Telmisartan and Aerosil200 in 1:3 ratio shows the release of 87.73% at the end of 1 hour.

Conclusion

Telmisartan solubility was enhanced by the surface solid dispersion technique using hydrophilic polymers like avicel PH101, alginic acid, and Aerosil200. Amongst the formulations prepared (F1-F9), F3 formulation containing Telmisartan, and Avicel PH101 in 1:3 ratio respectively was considered as optimized formulation in which percentage drug release was found to be 92.07% within 60 minutes in comparison with that of the pure drug dissolution of 35.06% only within 60 minutes. This effect may be due to fine particle size of telmisartan adsorbed over carriers resulting in a higher surface area of drug exposed to the dissolution media and improved wettability of the drug particles which contribute to high drug dissolution rate. The FT-IR study reveals that their no interaction between the drug and excipients can be used for preparation of telmisartan surface solid dispersion method.

Bibliography

1. Naga Aparna T. "Studies on enhancement of dissolution rate of Domperidone by surface solid dispersion technology". *International Journal of Research in Pharmacy and Chemistry* 1.2 (2011): 133-134.

2. Gamal Zayed ."Dissolution rate enhancement of ketoprofen by surface solid dispersion with colloidal silicon dioxide. *Unique Journal of Pharmaceutical and Biological Sciences* 2.1 (2014): 33-38.

3. Rahul M Patil. "Solid dispersion: strategy to enhance solubility". *International Journal of Pharmaceutical Sciences Review and Research* 8.2 (2011): 66-77.

4. T Kiran. "Surface solid dispersion of glimepiride for enhancement of dissolution rate". *International Journal of PharmTech Research* 1.3 (2009): 822-831.

5. Cassidy OE and Rouchotas C. "Comparison of surface modification and solid dispersion techniques for drug dissolution". *International Journal of Pharmaceutics* 195.1-2 (2000): 1-6.

6. Pinnamaneni NG., *et al*. "Formulation approaches for orally administered poorly soluble drugs". *Pharmazie* 57.5 (2002): 291-300.

7. Charumanee S., *et al*. "Improvement of dissolution rate of piroxicam by surface solid dispersions". *CMU Journal* 3.2 (2004): 77-84.

8. Chaulang G., *et al*. "Preparation and characterization of solid dispersion tablets of Furosemide with crospovidone". *Research Journal of Pharmacy and Technology* 1.4 (2008): 386-389.

9. Nokhodchi A., *et al*. "An Investigation on the solid dispersions of chlordiazepoxide". *International Journal of Biological Sciences* 3.3 (2007): 210-216.

10. Moneghini M., *et al*. "Processing of carbamazepine-polyethylene glycol 4000 solid dispersions with supercritical carbon dioxide: preparation, characterization and in vitro dissolution". *International Journal of Pharmaceutics* 222.1 (2001): 129-138.

11. Yi-Dong Yana., *et al*. "Novel valsartan-loaded solid dispersion with enhanced bioavailability and no crystalline changes". *International Journal of Pharmaceutics* 422.1-2 (2012): 202-210.

12. Li Di., *et al*. "Drug-like property concepts in pharmaceutical design". *Current Pharmaceutical Design* 15 (2009): 2184-2194.

13. Duncan QM Craig. "The mechanisms of drug release from solid dispersions in water-soluble polymers". *International Journal of Pharmaceutics* 231.2 (2002): 131-144.

14. Hemant N Joshi., *et al*. "Bioavailability enhancement of a poorly water-soluble drug by solid dispersion in polyethylene glycol-polysorbate 80 mixture". *International Journal of Pharmaceutics* 269.1 (2004): 251-258.

15. Toshio Oharaa., *et al*. "Dissolution mechanism of poorly water-soluble drug from extended release solid dispersion system with ethylcellulose and hydroxypropylmethylcellulose". *International Journal of Pharmaceutics* 302.1-2 (2005): 95-102.

Volume 2 Issue 1 January 2018