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Dissolution Enhancement of Telmisartan by Surface Solid Dispersion Technology

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ABSTRACT

Telmisartan is a well-known and widely used anti-hypertensive drug and it belongs to biopharmaceutical classification system (BCS) class II drug with low solubility and high permeability. The present study was aimed to enhance the solubility of telmisartan by surface solid dispersion technique using carriers like PVP K30 and aerosil 200 as adsorbent. The prepared formulations were characterized for percentage practical yield, drug content and *in vitro* drug release studies. Amongst the formulations prepared (F1-F4), F4 formulation consisting of telmisartan, PVP K30 and aerosil 200 in 1:2:2 ratios respectively was considered as optimized formulation in which percentage drug release was found to be 96.07% within 60 minutes in comparison with that of the pure drug dissolution of 45.90% 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. Also FT-IR spectroscopy studies were carried out in order to characterize the drug and surface surface solid dispersion and it revealed that there is no drug interaction with carriers.

Key words: Surface solid dispersion, PVP K30, Solvent evaporation method.

INTRODUCTION

Formulation of poorly soluble compounds for oral delivery now presents one of the most frequent and greatest challenges to formulation scientists in pharmaceutical industry (Sharma Daisy, 2009). Telmisartan is an Angiotensin II Receptor Antagonist, which is used in the prevention and treatment of Hypertension (Gosse P, 2006). One of the major problems with it is its low solubility in biological fluids, which results into poor bioavailability after oral administration (42%) and late onset of action. It also shows high first pass metabolism which further reduces the oral bioavailability. Surface solid dispersion technique has been used to increase the solubility, dissolution and consequently the bioavailability of much poorly water soluble drugs (Wienen W *et al.*, 2000). Formation of surface solid dispersion is a strategy that is used to reduce the agglomeration of the drug by increasing its surface area in a way that can help in increasing its dissolution rate (Vasconcelos T, 2007). The surface solid dispersions can overcome some of the shortcomings of the conventional solid dispersions (Shinde SS, 2010). The carriers used in surface solid dispersion are water insoluble, porous materials and hydrophilic in nature. The release of drug from the carrier material depends on hydrophilic nature, particle size, porosity and surface area of the carrier. Larger the surface area available for surface adsorption of the drug better is the release rate (Kausalya J, 2011).

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MATERIALS AND METHODS

MATERIALS

Telmisartan (A to Z Pharma Pvt. Ltd. Chennai), Chloroform (Merck Pvt. Ltd. Mumbai), PVP K30 (Merck Pvt. Ltd. Mumbai), Aerosil 200 (Merck Pvt. Ltd. Mumbai).

PREPARATION OF SURFACE SOLID DISPERSIONS (SSD)

The Surface Solid Dispersions of telmisartan were prepared by solvent evaporation technique using PVP K30 and aerosil 200 in 1:1:1, 1:1:2, 1:2:1 and 1:2:2 different weight ratios of drug, polymer and adsorbent respectively. The calculated amount of drug and PVP K30 were dissolved in 10ml of chloroform separately.

Then both the solutions were added to beaker containing aerosil 200 dissolved in 10ml of chloroform. The obtained slurry was subjected to heating at 61^0C using steam bath until the solvent (chloroform) evaporated completely. The resulting mass was transferred to desiccators containing Calcium chloride and stored until completely dry. The resulting solid mass was then pulverized in a mortar to get dry free flowing powder. The powders were then passed through a sieve no. 100 and *in-vitro* studies were performed (Kothawade S *et al.*, 2010).

EVALUATION OF SOLID DISPERSION

1. PERCENTAGE PRACTICAL YIELD

The prepared surface solid dispersions were weighed accurately and it was taken as theoretical yield. Then the percentage practical yield was calculated by using the formula as follows:

$$\text{Percentage of practical yield} = \frac{\textbf{practical yield}}{\textbf{theoretical yield}} \times 100$$

2. DRUG CONTENT

Equivalent weight of SSD containing 1mg drug was weighed accurately and transferred in 10ml standard flasks and volume was made up to 10ml with methanol. Take 1ml from above the solution in 10ml standard flasks and volume made up to 10ml with methanol. The solution was filtered and analyzed for their drug content spectrophotometrically by measuring absorbance at 296nm.

Percentage of drug content was calculated by following formula:

$$\% \text{ of Drug Content} = \frac{\text{Observed value}}{\text{Actual Value}} \times 100$$

3. FOURIER TRANSFORM INFRARED (FT-IR) STUDIES

FTIR spectra of the pure drug, PVP K30, aerosil 200 and SSDs were all carried out. The IR spectra were recorded using Infra-red Spectrophotometer (Thermo-IR 200 FTIR spectrophotometer). Potassium bromide pellet method was employed and background spectrum was collected under identical conditions. Each spectrum was derived from 16 signals average scans collected in the range of 500-3000 cm $^{-1}$ at the spectral resolution of 20 cm^{-1}.

4. *IN VITRO* DISSOLUTION STUDIES

The release of telmisartan from surface solid dispersions was determined using USP type II (paddle type) dissolution apparatus. The dissolution test was performed using pH7.5 buffer as dissolution media at 37 ± 0.5 ^{0}C with 75 rpm for 60 minutes. A sample of each preparation equivalent to 10 mg of drug was added to dissolution medium. A 5ml aliquot was withdrawn at different time intervals (15, 30, 45, 60 minutes) and filtered and each sample was replaced with 5ml of fresh dissolution medium. The filtered solutions were suitably diluted to 10ml with dissolution media. Samples were analyzed for its drug content spectrophotometrically by measuring the absorbance against blank at 296nm (Ahuja N *et al.*, 2007). Percent of telmisartan dissolved at various time intervals was calculated.

RESULTS AND DISCUSSION:

1. PERCENTAGE PRACTICAL YIELD:

Four formulations of surface solid dispersions of telmisartan were prepared and weighed accurately. Then the percentage practical yield was calculated by using the formula as follows:

$$\text{Percentage of practical yield} = \frac{\textbf{practical yield}}{\textbf{theoretical yield}} \times 100$$

When compared to other formulations, F4 formulation showed highest Percentage practical yield i.e., 90%.

Table.1 COMPOSITION OF SSDs

S.NO	DRUG : PVPK30 : AEROSIL200	DRUG (mg)	PVP K30 (mg)	AEROSIL200 (mg)
1	1:1:1	500	500	500
2	1:1:2	500	500	1000
3	1:2:1	500	1000	500
4	1:2:2	500	1000	1000

Table.2 FORMULATION CODE

S.NO	DRUG : PVPK30 : AEROSIL 200	FORMULATION CODE
1	1:1:1	F1
2	1:1:2	F2
3	1:2:1	F3
4	1:2:2	F4

Table.3 Percentage practical yield of SSDs

S.NO	FORMULATION CODE	% PRACTICAL YIELD
1	F1	80.02%
2	F2	85.20%
3	F3	87.50%
4	F4	90.01%

Table.4 Percentage drug content of SSD

S.NO	FORMULATION CODE	% DRUG CONTENT
1	F1	89.01%
2	F2	91.30%
3	F3	93.60%
4	F4	94.01%

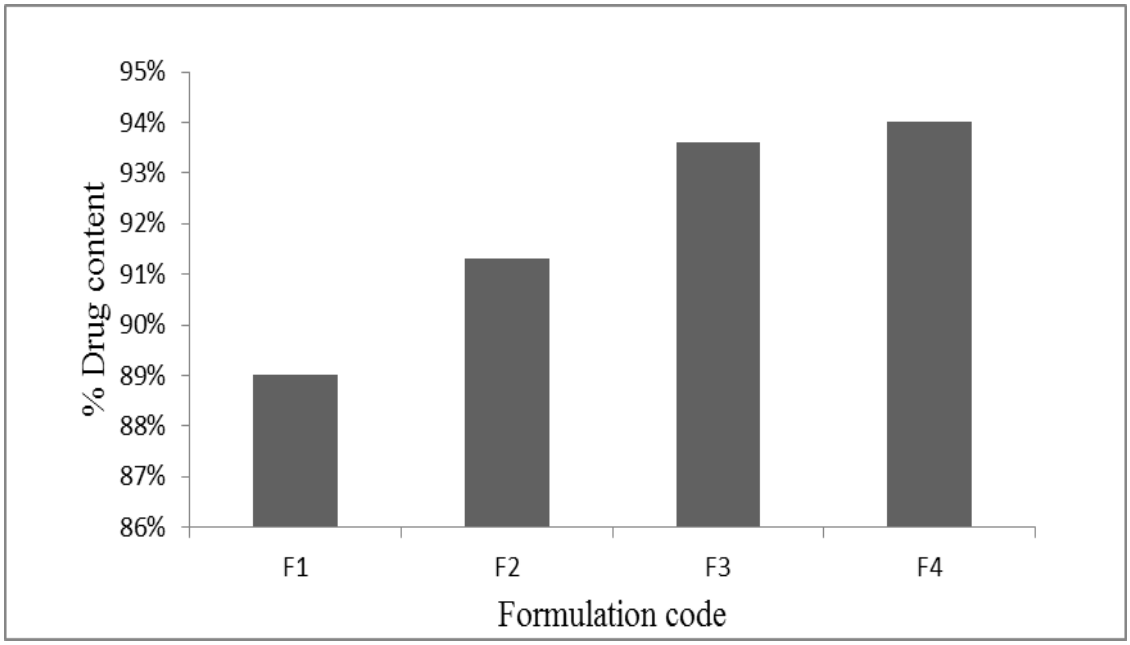

Figure.1 Bar diagram for percent drug content of SSD

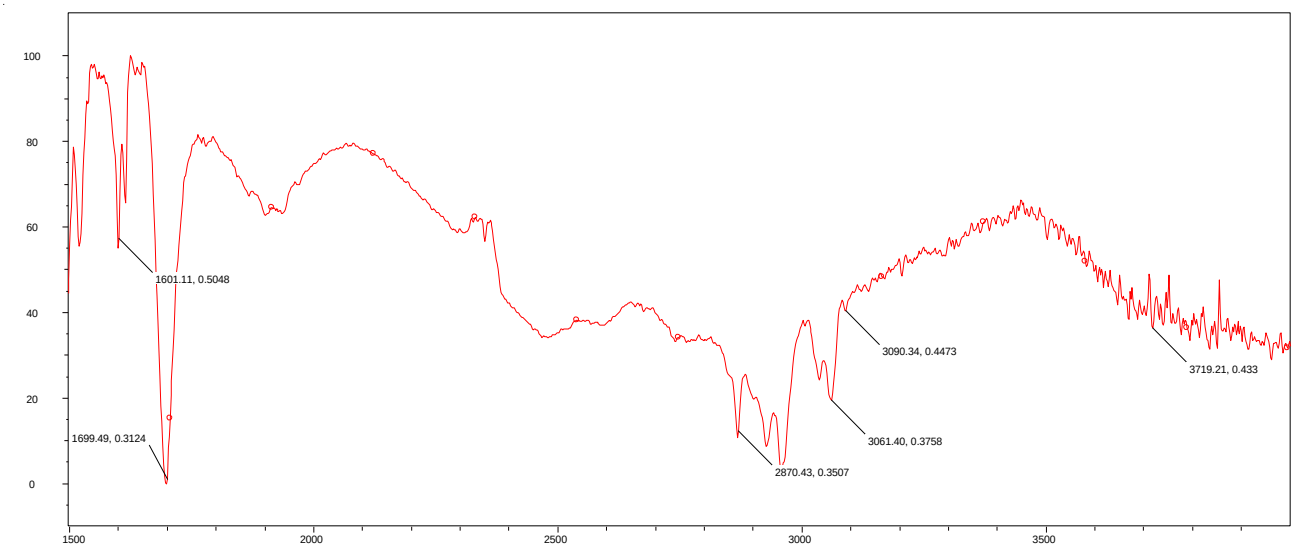

Figure.2 FT-IR spectra of pure drug (Telmisartan)

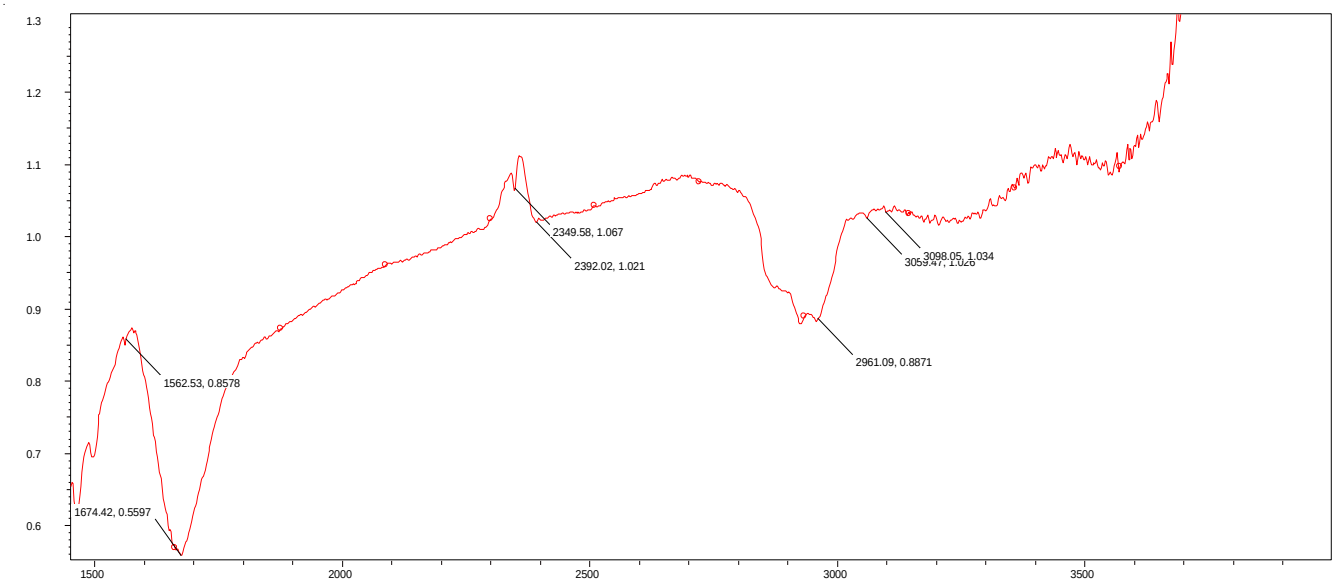

Figure.3 FT-IR spectra of Surface solid dispersions

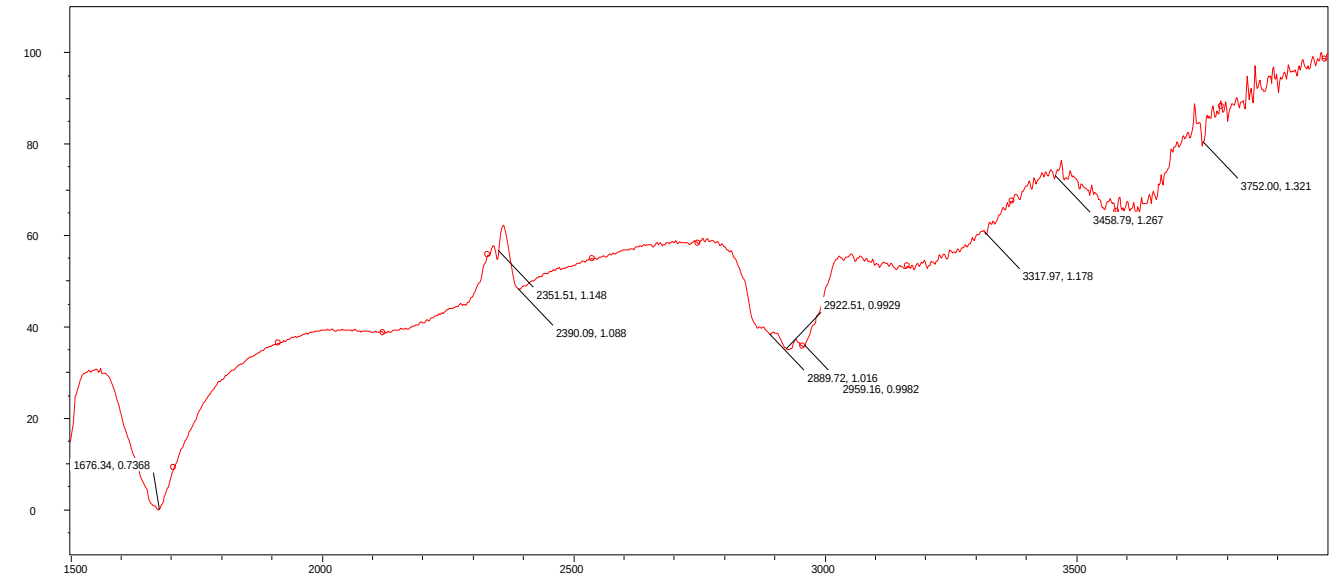

Figure.4. FT-IR spectra of PVP K30

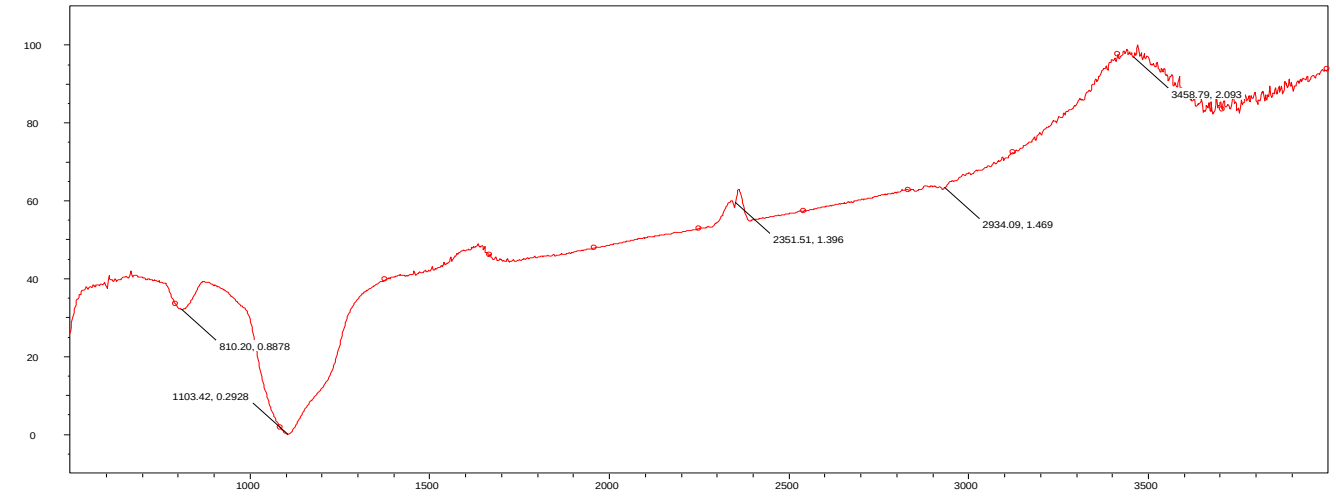

Figure.5. FT-IR spectra of Aerosil 200

Table.5 *In-vitro* dissolution profiles of telmisartan surface solid dispersions

S.NO.	TIME (min)	% CUMULATIVE DRUG RELEASE				
		PURE DRUG	F1	F2	F3	F4
1	15	17.10	25.20	37.62	49.14	59.76
2	30	38.20	41.90	50.10	61.47	71.67
3	45	42.50	51.49	68.17	75.61	85.47
4	60	45.90	64.80	77.92	86.65	96.07

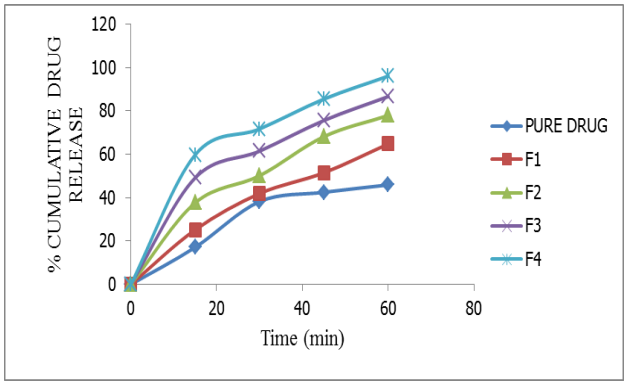

Figure.6. Dissolution profile of surface solid dispersions of telmisartan

2. PERCENTAGE DRUG CONTENT

From the results, it was observed that percentage loss of drug content during preparation was very low. Low correlation values in percent drug content ensured uniformity of drug in each batch. Thus it was found that the ratios and method used to prepare surface solid dispersions have shown no effect on percent drug content.

3. Fourier Transform Infrared (FT-IR) Studies

From the FTIR data, it was found that there were no new bands observed in the spectrum, which confirms that no new chemical bonds were formed between the drug and the excipients. The FTIR spectra were shown in figures 2, 3, 4 and 5.

4. *IN-VITRO* DISSOLUTION STUDIES

From the results, it was found that the percentage drug release of pure telmisartan was very low and only 45.9% dissolved in 60 minutes. Out of four formulations, F4 formulation showed the highest percentage drug release i.e., 96.07% within 90 minutes when compared to that of pure drug. However all the four formulations gave a significant improvement in the solubility as compared to that of the pure drug.

CONCLUSION

Telmisartan solubility was enhanced by the surface solid dispersion technique using carriers like PVP K30 and aerosil 200 as adsorbent. Amongst the formulations prepared (F1-F4), F4 formulation containing telmisartan, PVP K30 and aerosil 200 in 1:2:2 ratios respectively was considered as optimized formulation in which percentage drug release was found to be 96.07% within 60 minutes in comparison with that of the pure drug dissolution of 45.90% 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.

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