ISSN PRINT 2319 1775 Online 2320 7876

Research paper UGC CARE Listed (Group -I) Journal Volume 11,S Iss 3, Dec 2022

Research Article

SOLUBILITY ENHANCEMENT OF TELMISARTAN BY VARIOUS TECHNIQUES

Sidhartha Parida[1], Nihar Ranjan Kar[1]*, Sumita Singh[2], Sradhanjali Patra[2], Hrudesh Priyadarshan Sahoo[1], Binayak Mishra[1], Monalisa Gochhi[3]

[1]Centurion University of Technology and Management,Odisha,India
[2]University Department of Pharmaceutical Sciences, Utkal University, Vani Vihar, Bhubaneswar, Odisha -751004, India
[3]Sri Jayadev College of Pharmaceutical Sciences,Naharkanta,Bhubaneswar,Odisha,India

***Corresponding Author Details:-**
Dr. Nihar Ranjan Kar
Assistant Professor,
School of Pharmacy,
Centurion University of Technology and Management,
Odisha, India
Phone No- +91-9439511837
E.Mail Id.- nihar_795@rediffmail.com
ORCID ID- 0000-0001-9128-2506

ABSTRACT: -

Aim/Background:-The objective of present research was aimed to intensify the bioavailability of drug Telmisartan by enhancing its solubility. It is a drug that belongs to BCS class II and has high permeability but low solubility, which is an anti-hypertensive agent. As it is low soluble its generally showing poor bioavailability. **Materials/Methods:-**An effort was made to improve dissolution rate through the preparation of solid dispersions of Telmisartan with water soluble carries like polyethylene glycol and beta cyclodextrin by solvent evaporation method, melt evaporation method, kneading method. Nine formulation like were prepared in the ratio of 1:1, 1:3,1:5(drug : polymer). **Results/Discussion:**-Evaluation tests like physiochemical parameters, wettability and *in vitro* dissolution study were done accordingly. All of the polymers were found to be efficient in speeding the dissolution of Telmisartan in solid dispersions as compared to the pure drug. Additional FT-IR spectroscopy, different scanning calorimetry, and X-ray diffractometry investigations were carried out to characterise the drug and solid dispersion. Formulation F9 was found as best among all.

KEYWORDS:-Telmisartan, Solid dispersion, Polyethylene glycol, β-Cyclodextrin, Bioavailability

INTRODUCTION: - The treatment and prevention of hypertension with the use of Telmisartan, an angiotensin II receptor antagonist. Telmisartan is a class II medication according to the BCS classification due to its low solubility and high permeability. One of the main problems with the medicine is its limited solubility in biological fluids, which results in

ISSN PRINT 2319 1775 Online 2320 7876

Research paper UGC CARE Listed (Group -I) Journal Volume 11,S Iss 3, Dec 2022

poor bioavailability after oral treatment. In aqueous conditions, telmisartan has a relatively low solubility (0.078 mg/ml in water). Since Telmisartan's biological half-life was only 24 hrs, its absolute bioavailability after oral treatment was insufficient. It ranged from 42 to 58 %. Telmisartan's poor dissolution and weak solubility alter its bioavailability. Therefore, to achieve therapeutic goals, Telmisartan's water solubility and dissolution must be improved. Numerous methods have been developed to improve the solubility and dissolving of medicines. When the drug is incorporated into a polymeric matrix that is water soluble, the solid dispersion is a way to achieve this, especially for medications that are poorly aqueous soluble. This study investigated the solubility and bioavailability of Telmisartan when conjugated with various carriers using a variety of approaches. Other evaluation methods were utilised in addition to this study on solubility and dissolution to determine the physical and chemical properties of solid dispersions and physical mixtures in contrast to pure drugs.[1]

Solid Dispersion: - Solid dispersions are defined as "a dispersions of one or more active ingredients in an inert carrier or matrix in solid state prepared by different methods".[2]
The solid dispersions can be prepared by the following techniques:
1. Physical mixing method
2. Solvent evaporation method (common solvent method)
3. Melting Method (Fusion Method)
4. Melt evaporation method (melting solvent method)
5. Kneading method (inclusion method)
6. Melt Extrusion method
7. Melt Agglomeration Process
8. Super critical fluid technology

Mechanism: Solid dispersions are prepared, to reduce the particle size and increase the surface area of a poorly water soluble drugs (BCS-II and BCS-IV), which leads to enhancement of the dissolution and solubility of the drug.[3]

MATERIALS & METHODS

MATERIALS

Free Telmisartan samples were provided by Mumbai-based Macleods Pharma Pvt. Ltd. The polymers, including β-CD ,PEG-6000 were supplied by Dr. Reddy's Lab in Hyderabad. Conc. HCl was bought from SD Fine-Chem Ltd. in Mumbai, and all other chemicals were of analytical purity.

METHODS

Formulation of Solid Dispersion:-

I. Melt evaporation method:- The solid dispersion of telmisartan with PEG 6000 was made using the melt evaporation method in a range of drug:PEG 6000 ratios (1:1, 1:3, and 1:5). The telmisartan was dissolved in 0.1N HCL to produce a transparent solution. PEG 6000 was then evaporated in fine particle form at 60 °C over a water bath to remove the solvent. Once the dried bulk had reached a uniform consistency, it was ground up and passed through an 80-µm sieve.[4]

II. Solvent evaporation method: - The solid dispersion of Telmisartan with PEG 6000 was made using the solvent evaporation technique in a range of drug-to-PEG 6000 ratios (1:1, 1:3, and 1:5). Telmisartan was dissolved in methanol to yield a clear solution. PEG 6000 was then

ISSN PRINT 2319 1775 Online 2320 7876

Research paper UGC CARE Listed (Group -I) Journal Volume 11,S Iss 3, Dec 2022

evaporated in fine particle form at 60 °C over a water bath to remove the solvent. Once the dried bulk had reached a uniform consistency, it was ground up and passed through an 80-µm sieve.[5]

III. Kneading method: - In a glass mortar, β-CD and water were mixed to make a consistent paste. The drug Telmisartan was then progressively added to the paste, and the mixture was completely combined for an hour. To maintain the paste's consistency during this time, the water content was empirically changed. The paste that had been made was dried under vacuum for 24 hrs. After passing through a special sieve no. 80, the dried powder was kept in a desiccators [6].

The Drug and Polymer Content of all formulations has been shown in the Table-1.

Table -1:- Composition of all Formulations.

Formulation	Telmisartan	PEG6000 (mg)	β-cd (mg)	Followed Method
F1	500	500	-	Melt evaporation
F2	500	1500	-	Melt evaporation
F3	500	2500	-	Melt evaporation
F4	500	500	-	solvent evaporation
F5	500	1500	-	solvent evaporation
F6	500	2500	-	solvent evaporation
F7	500	-	500	Kneading
F8	500	-	1500	Kneading
F9	500	-	2500	Kneading

Micromeritics Study Of Pure Drug

Bulk density – It is characterised as the mass of power by bulk volume.[7]

Method: A precisely weighted 2gm of powder sample is cautiously introduced to a 100ml measuring cylinder. The initial volume is noted.

Bulk density— Wt. of sample (gm)/ bulk volume (ml)

Tapped density – The proportion of weight of powder sample to the tapped volume.[8]

Method: After determining bulk density, the measuring cylinder was tapped on hard surface for 100 times and volume occupied was noted.

Tapped density—wt. of sample (gm) / tapped volume (ml)

Angle of Repose – This is the widest possible angle by powder pill and a horizontal plane.[9]

Method: It is determined by funnel method. The graph paper was placed on a level, horizontal surface with a tight funnel placed above it, with the funnel's tip at the desired height (h). The powder is delicately poured through the funnel until the apex of the conical pile just brushes the tip. The radius (r) of the base of the conical pile was calculated.

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

Hausner's ratio – It is characterize the flow of nature of powder and granules.[10] It is beneficial if the HR ratio is less than 1.25; it is bad if it is greater than 1.25.

Compressibility Index – Based on how much powder might create an arch in a hopper and how easy that arch might be broken, it can be determined. It describes how granules and powders are made. The relationship between it and particle size, cohesiveness, and relative flow rate is unbreakable.[11]

ISSN PRINT 2319 1775 Online 2320 7876

Research paper UGC CARE Listed (Group -I) Journal Volume 11,S Iss 3, Dec 2022

Compressibility Index (%) – (Tapped density – Bulk density) / tapped density x 100

Calibration Curve Of Pure Drug:- The first step in preformulation study is to establish an analytical method so that all future measurement can be quantitative. 1mg/ml solution of Telmisratan was prepared with distilled water. The prepared solution was scanned for λmax against the corresponding medium as blank in the spectral range of 200-270nm. The spectrums were recorded and from the spectrum λmax was determined. Then linearity was checked by preparing calibration curve by taking different diluted solutions in the medium. These results were represented in the Table-2 and Figure-1.[12]

Table -2:-Calibration curve of Telmisartan with water.

Medium	**λmax**
Distilled water	216
Concentration(mcg/ml)	**Absorbance**
0	0
2	0.024
4	0.050
6	0.072
8	0.095
10	0.120

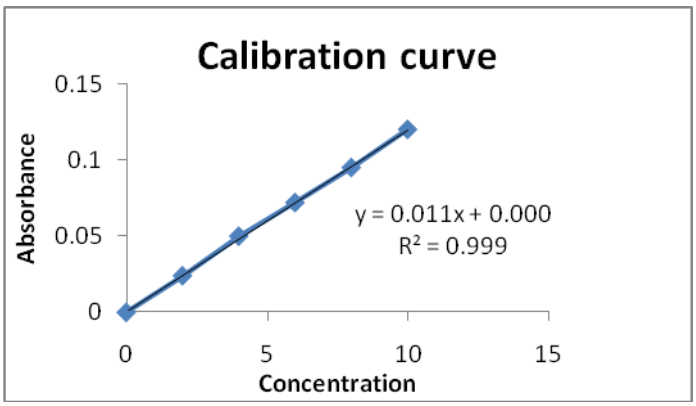

Figure -1:-Calibration curve of Telmisartan with Water.

Calibration curve of Telmisartan and β-cyclodextrin with water:- The second step in preformulation study is to establish an analytical method so that all future measurement can be quantitative. 1mg/ml solution of Telmisartan with beta cyclodextrin was prepared with distilled water. The prepared solution was scanned for λmax against the corresponding medium as blank in the spectral range of 200-300nm.The spectrums were recorded and from the spectrum λmax was determined. Then linearity was checked by preparing calibration curve by taking different diluted solutions in the medium. These results were represented in Table-3 and Figure-2.[13]

Table - 3:- Calibration curve of Telmisartan with β-cyclodextrin.

Concentration (mcg/ml)	**Absorbance**
0	0
2	0.022
4	0.041

ISSN PRINT 2319 1775 Online 2320 7876

Research paper UGC CARE Listed (Group -I) Journal Volume 11,S Iss 3, Dec 2022

6	0.064
8	0.085
10	0.109

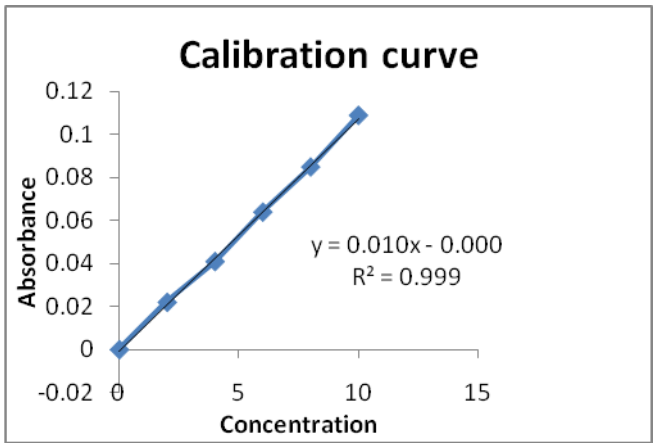

Figure - 2:– Calibration curve of Telmisartan with β-CD.

Percentage(%) of Yield :- The percentage of yield was carried out to know the any drug lose during formulation. Yield for all formulations were within the range of 61.66% - 95.91%.[14]

% Yield= [practical weight of the formulation / (Theoretical weight of Drug + Weight of polymer)] x 100

Wettability study: - A glass funnel was filled with around 300 mg of the medication's solid dispersion powder (55m). 10 mg of methylene blue powder was applied to the surface of the test sample. The funnel was lowered into a beaker of water, keeping the water's surface there at the same level as the powder inside. It was calculated how long it would take to moisten the methylene powder. The observations were calculated for its wettability.[15]

Aqueous solubility of formulations:-Accurately weighed 50mg, 100mg,150mg of solid dispersions were carefully transferred into a clean, dry 25ml conical flask containing 25ml of distilled water. The flask was then shaken for 2hrs through rotary shaker, and the contents of flask were filtered through a filter paper (whattman no 41), diluted suitably and the drug content was determined at maximum wavelength with distilled water using UV-Visible spectrophotometer.[16]

Drug Content of Formulation:-Accurately weighed formulations equivalent to 25mg of Telmisartan was carefully transferred in a clean dry 25ml volumetric flask and volume was made up to 25ml with distilled water. The flask was then shaken and content of flask were filtered on a filter paper (whattman no 41), diluted suitably and the drug content as determined at maximum wavelength with distil water using UV-Visible spectrophotometer.[17]

FTIR Study

The drug and excipient(s) compatibility study was carried out by doing FTIR study. Each dosage (5 mg) was combined with approximately 100 mg of potassium bromide and compressed into discs at a pressure between 10,000 and 15,000 pounds per square inch. The IR spectra were captured using an infrared spectrometer (Bruker α , Mumbai).[18]

Differential Scanning Calorimetry (DSC)

In the preformulation phase of the development of solid dosage forms, it is crucial to assess any potential incompatibilities between an active pharmaceutical ingredient and various

ISSN PRINT 2319 1775 Online 2320 7876

Research paper UGC CARE Listed (Group -I) Journal Volume 11,S Iss 3, Dec 2022

excipients. The differential scanning calorimeter is advantageous because it can immediately determine potential incompatibilities through changes in appearance, shifts in melting endotherms and exotherms, and/or adjustments in the associated reaction enthalpies (DSC TA-Lab-METLLER STARe SW 12.10). Both complex DSC thermograms and pure drug thermograms were taken. The instrument was calibrated with pure indium (99.99%). 5mg samples were enclosed inside a flat-bottomed aluminium pan. The pan was inserted into the DSC equipment and scanned between 15^0 C and 300^0 C at a rate of 20°C/min. Dry nitrogen was used as a carrier gas with a flow rate of 10 ml/min to totally counteract the oxidative and pyrolytic effects. Melting and transition points were measured using the instrument's software. A DSC study was carried out for the polymers and telmisartan drug combination.[19]

X-Ray Diffractometry (XRD)

Sample XRD spectra were recorded using a high-power powder x-ray diffractometer (D2 Phaser, BRUKER, AXS Inc., Germany). The crystal structure of the pure drug and solid dispersion formulation were examined by analysing its X-Ray diffraction patterns.[20]

In vitro **dissolution study:-** 500ml of distilled water medium positioned in the dissolution vessel and temperature was maintained to $37^o \pm 0.5^o$ C. 40mg of Telmisartan was added to dissolution medium and paddle was allow to rotate at 100 rpm. At regular intervals, 1 ml of the media was sampled, and 1 ml of more medium was added to keep the dissolving medium's volume constant. The samples were then examined for drug content using a UV-Visible spectrophotometer at the respective max, which is 216 nm, using the medium as a blank.[21]

RESULT AND DISCUSSION

Micromeritic Study of Pure Drug

From the micromeritic study of pure drug, it can be concluded that the pure drug has poor flow characteristics, as seen by the Compressibility Index and Angle of repose tests which has shown in Table-4. Among all formulations, the Compressibility Index and Angle of repose data of the optimal formulation (F9) is found to have good flow properties which has shown in Table-5.

Table - 4: Micromeritic study of pure drug.

Parameter	Result
Bulk density	o.256gm/ml
Tapped density	0.384gm/ml
Carr's index	33.33%
Hausner's ratio	1.5
Angle of repose	30.45^0
Melting point	260^0C
Assay	99%

Table -5:- Micromeritic studies of best formulation(F9).

ISSN PRINT 2319 1775 Online 2320 7876

Research paper UGC CARE Listed (Group -I) Journal Volume 11,S Iss 3, Dec 2022

Parameters	Pure Drug	F9
Bulk density	0.256gm/ml	0.333gm/ml
Tapped density	0.384gm/ml	0.416gm/ml
Compressibility Index	33.33%	19.9%
Angle of repose	30.45^0	40°
Hausner 's ratio	1.5	1.2

Percentage(%) of Yield :- From the above experiment, it can be concluded that % of Yield of all formulations were within the range of 42% - 97% but the formulation F9 has shown highest % of yield of 97% , which has been shown in Table-6.

Table -6:-%Yield value of all Formulations.

Formulation Code	Theoretical Amount (Mg)	Practical Amount (Mg)	Yield
F1	1000	420	42%
F2	2000	1500	75%
F3	3000	2350	78.33%
F4	1000	720	72%
F5	2000	1600	80%
F6	3000	2660	88.66%
F7	1000	380	76%
F8	2000	1750	87.5%
F9	3000	2910	97%

Wettability study: - From Wettability studies it was found that F9 shows less wetting time (11 seconds) than other formulations and pure Telmisartan (8141 seconds) which has been shown in Table-7.

Table -7:- Wetting time of pure drug and F1-F9.

Formulation Code	Wetting Time(sec)
Pure drug	8141
F1	27
F2	18
F3	15
F4	28
F5	17

ISSN PRINT 2319 1775 Online 2320 7876

Research paper UGC CARE Listed (Group -I) Journal Volume 11,S Iss 3, Dec 2022

F6	24
F7	18
F8	12
F9	11

Aqueous solubility of formulations:- To speed up the solubility and dissolution of the water-insoluble drug Telmisartan, solid dispersions of the drug were created utilising water-soluble polymers such Polyethylene glycol (PEG 6000) and Beta Cyclodextrin. In the ratios of 1:1, 1:3, and 1:5, different formulations of Telmisartan Solid dispersions were created (Drug : Carrier). From solubility studies it was found that F9 shows highest solubility (72.91mg/ml) than other formulations and pure Telmisartan (0.00035 mg/ml).

Drug Content of Formulation:- from the above experiment, it can be concluded that the drug content of all formulations ranges from 91.08%-97.30% which are within the permissible range , among all highest drug content was shown by formulation F2 that is 97.30% which can be shown in the Table-8.

Table -8:- Drug content of formulations.

Formulations	Drug Content(%)
F1	91.08
F2	97.30
F3	95.62
F4	93.98
F5	93.24
F6	97.18
F7	92.12
F8	91.80
F9	92.76

FTIR Study The FT-IR spectra of pure Telmisartan showed sharp peak at 1696.47cm $^{-1}$ (C=O stretching vibration), 1268.25 cm^{-1} (C-N stretching vibrations), 2891.42 cm^{-1} respectively. From the FT-IR studies, it is indicated that no interaction occurred in solid dispersion of Telmisartan, PEG 6000, β-CD which was shown in Figure-3-7 and 8.

ISSN PRINT 2319 1775 Online 2320 7876

Research paper UGC CARE Listed (Group -I) Journal Volume 11,S Iss 3, Dec 2022

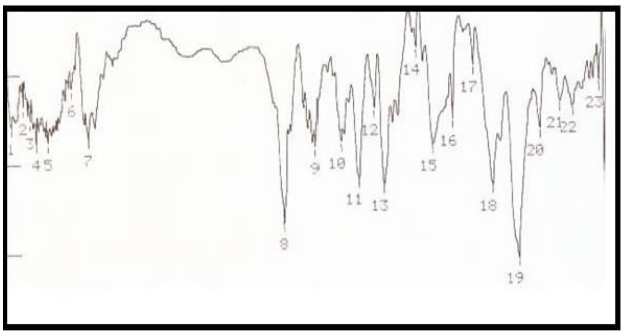

Figure - 3:-FTIR spectrum of Telmisartan.

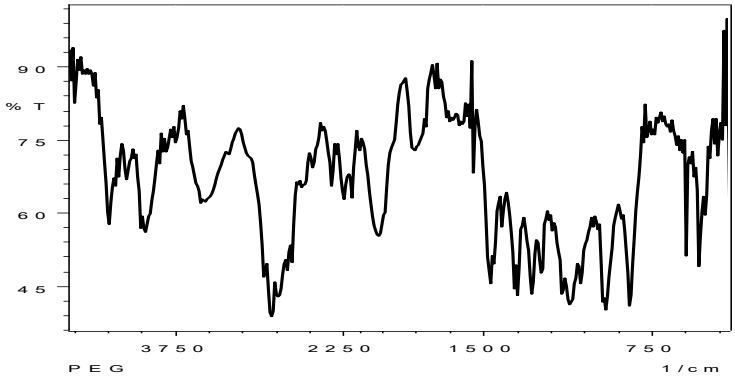

Figure -4:- FTIR Spectrum of PEG 6000.

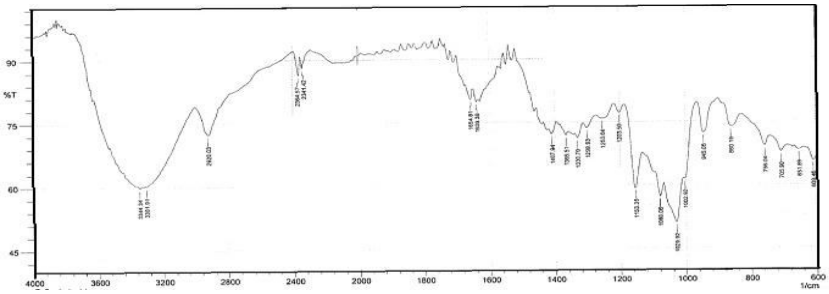

Figure -5:- FTIR spectrum of ß-CD.

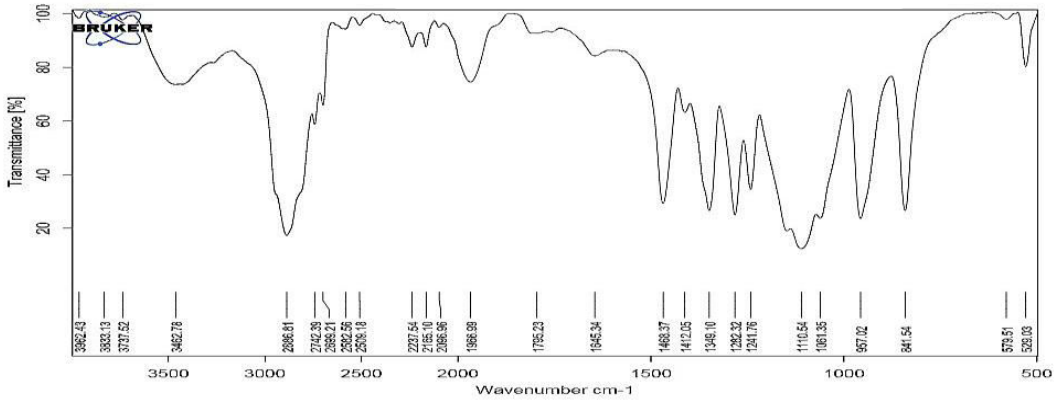

Figure -6:- FT-IR Spectrum of Telmisartan and PEG 6000.

ISSN PRINT 2319 1775 Online 2320 7876

Research paper **© 2012 IJFANS. All Rights Reserved, UGC CARE Listed (Group -I) Journal Volume 11,S Iss 3, Dec 2022**

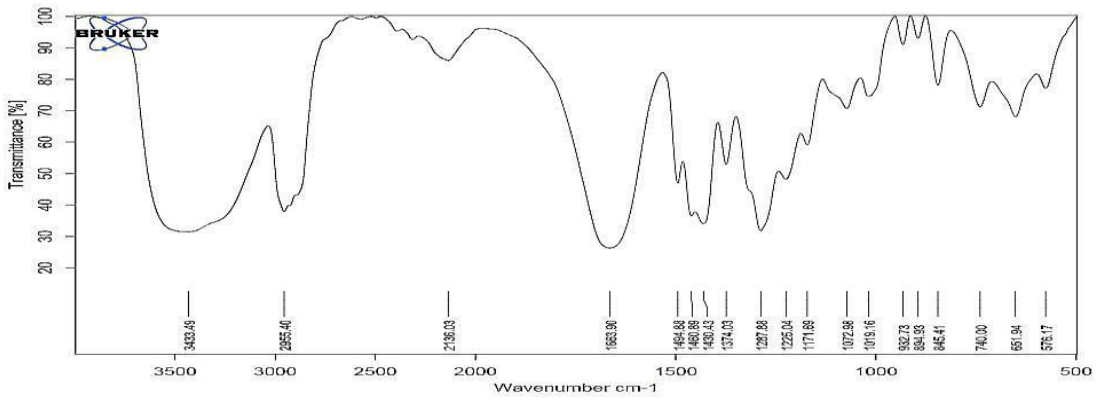

Figure -7:- FT-IR Spectrum of Telmisartan and β-CD.

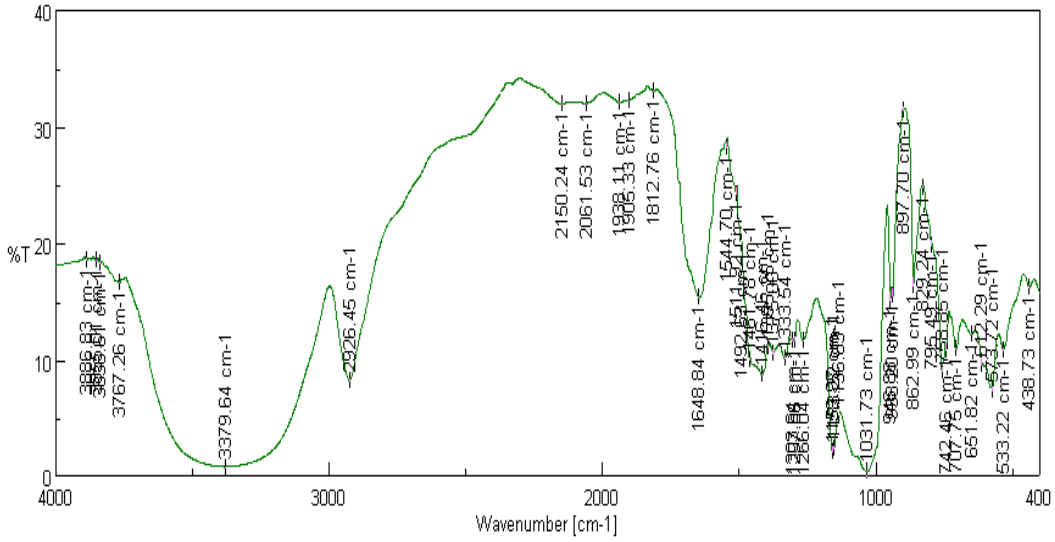

Figure -8:- FT-IR Spectrum of Best Formulation (F9).

DSC Study: - The DSC analysis of the pure drug revealed one distinct endothermic peak at 270.43^0 C, which was Telmisartan. The DSC curve of F9 displayed two endothermic peaks, a narrow peak at 270.13^o C that corresponded to Telmisartan and a sharp peak at 94.14^o C that corresponded to Beta cyclodextrin.This result showed there was no interaction between drug-excipient or excipient-excipient which can be shown in the Figure-9- 13 and 14.

ISSN PRINT 2319 1775 Online 2320 7876

Research paper **© 2012 IJFANS. All Rights Reserved, UGC CARE Listed (Group -I) Journal Volume 11,S Iss 3, Dec 2022**

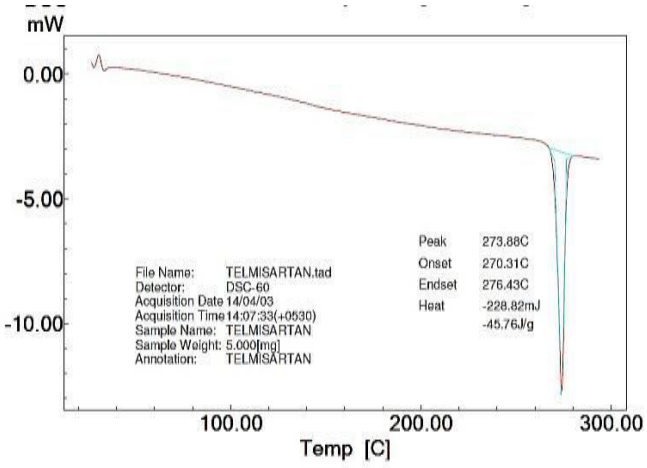

Figure -9:- DSC Thermogram of Telmisartan.

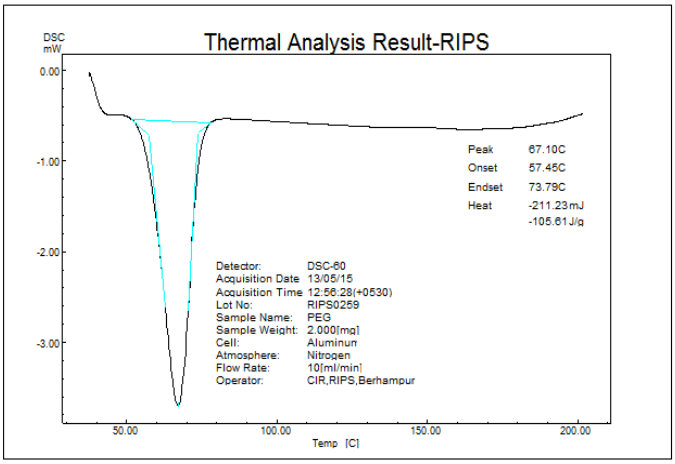

Figure -10:- DSC Thermo gram of PEG 6000.

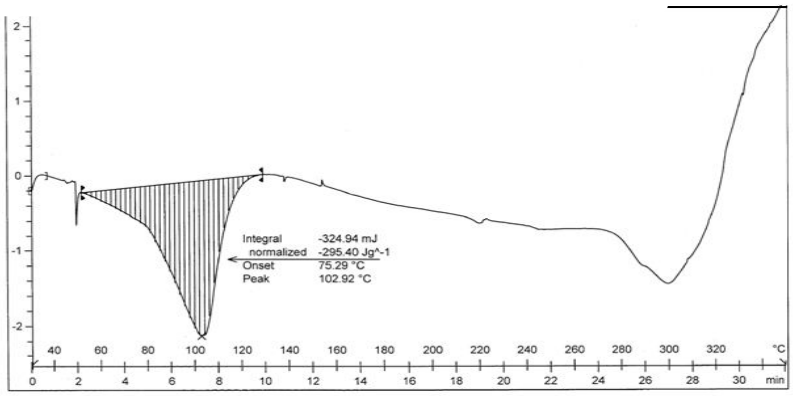

Figure -11:-DSC Thermo gram of β-CD.

ISSN PRINT 2319 1775 Online 2320 7876

Research paper UGC CARE Listed (Group -I) Journal Volume 11,S Iss 3, Dec 2022

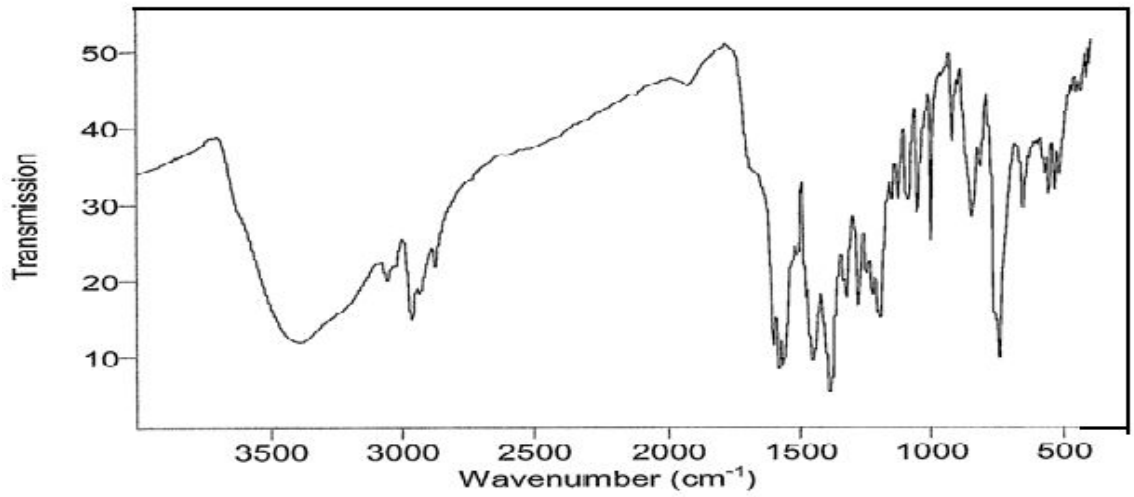

Figure -12:- DSC Thermo gram of Telmisartan and PEG 6000.

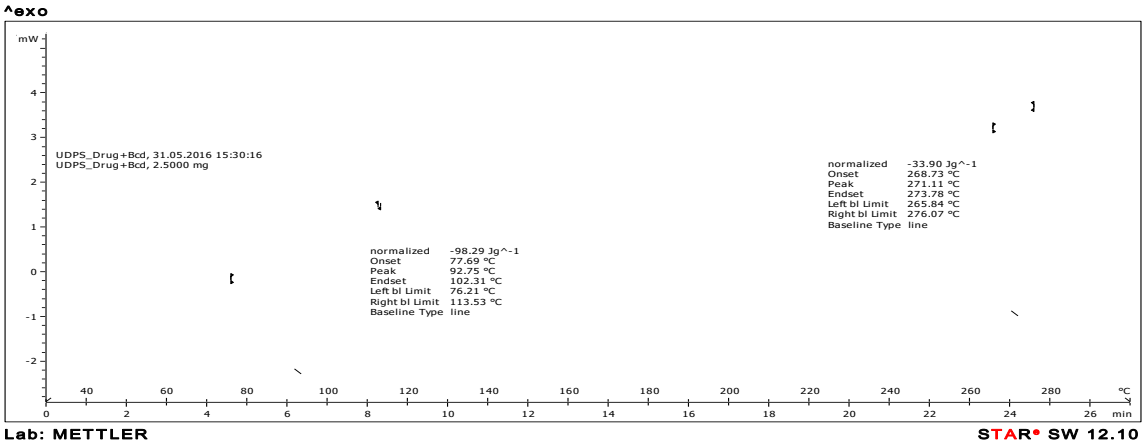

Figure -13: - DSC Thermo gram of Telmisartan and β-CD.

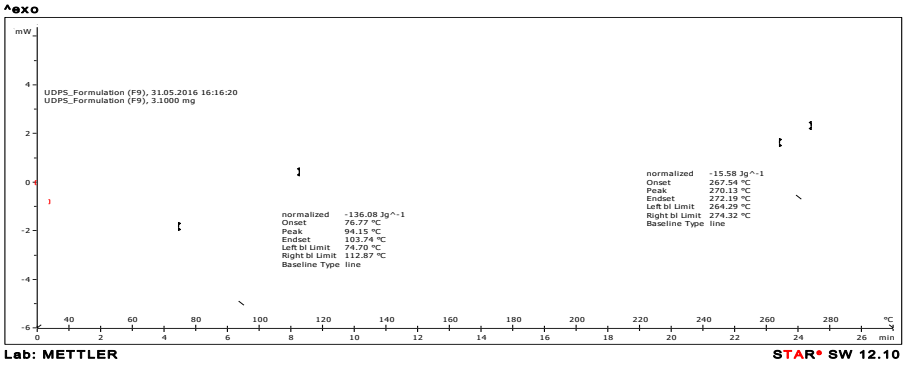

Figure -14: - DSC Spectrum of Best Formulation (F9).

ISSN PRINT 2319 1775 Online 2320 7876

Research paper UGC CARE Listed (Group -I) Journal Volume 11,S Iss 3, Dec 2022

XRD STUDY: - The pure drug's X-ray diffraction (XRD) results revealed certain distinctive peaks at the diffraction angle, pointing to the drug's presence as a crystalline substance. The best formulation (F9) displayed all of the drug's peaks, although their intensity was diffused in comparison to that of the pure substance. The outcome shows that the medication in solid dispersion is more amorphous than the pure drug. As a result, there was an increase in the drug's dissolution.The result of the study can be shown in the Figure-15-19 and 20.

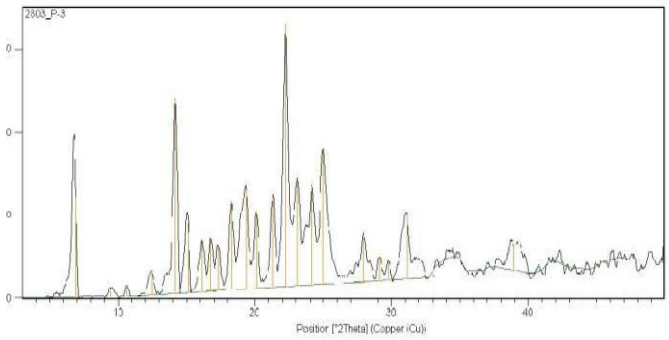

Figure -15:- XRD Spectrum of Telmisartan.

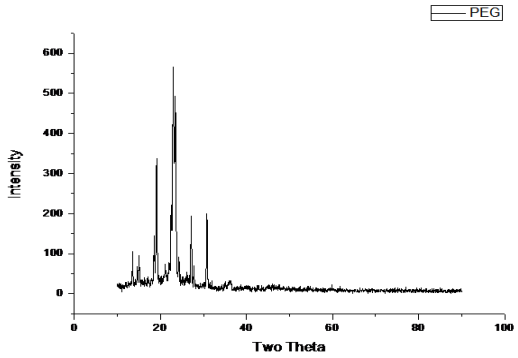

Figure -16 :-XRD spectrum of PEG 6000.

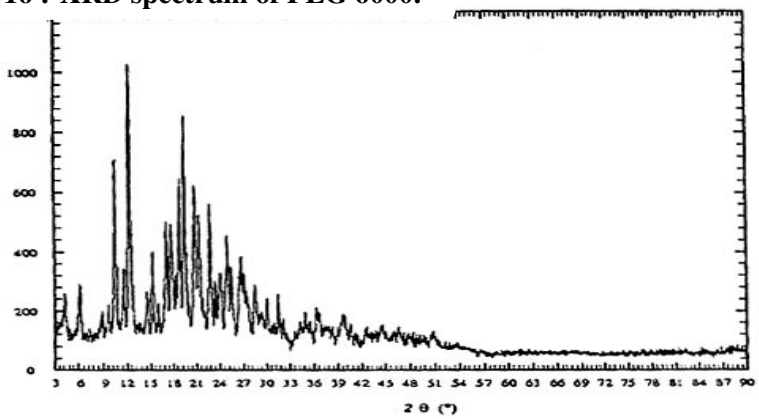

Figure -17:- XRD spectrum of β-CD.

ISSN PRINT 2319 1775 Online 2320 7876

Research paper UGC CARE Listed (Group -I) Journal Volume 11,S Iss 3, Dec 2022

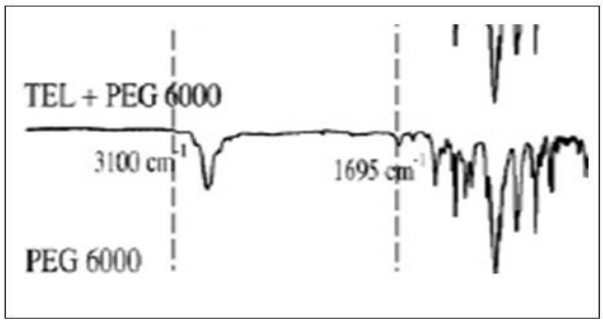

Figure -18:- XRD Spectrum of Telmisartan and PEG 6000.

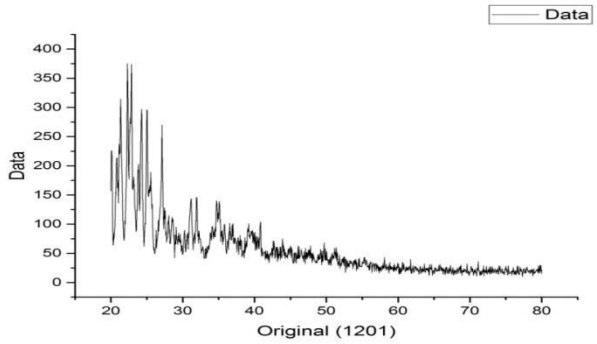

Figure -19:- XRD Spectrum of Telmisartan and β-CD.

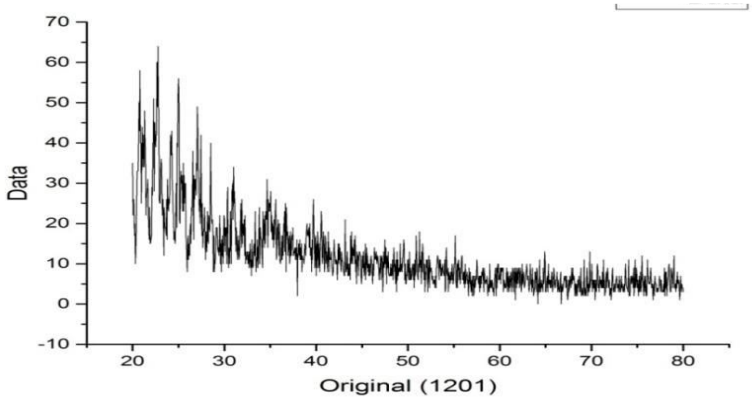

Figure -20:- XRD spectrum of Best Formulation (F9).

***In-Vitro* Drug Release Study: -** From the dissolution studies of all formulations, F9 (Drug : β-CD in 1:5 ratio, 97.74 % in 15 min) shows highest % of drug release than other formulations and pure drug(43.12 %,15 min) which can be shown in the Table-9 and Figure-21. As the R^2 -value is more than 0.8 value, so it can be predicted that, the system release suits both first order and zero order kinetics but more interpredictable value shows first order release kinetics which can be shown in the Table 10 and 11 and Figure-22.

Table -9:- Dissolution profile of pure drug.

ISSN PRINT 2319 1775 Online 2320 7876

Research paper UGC CARE Listed (Group -I) Journal Volume 11,S Iss 3, Dec 2022

Time (min)	%DR
0	0
5	16.75
10	24.12
15	43.12

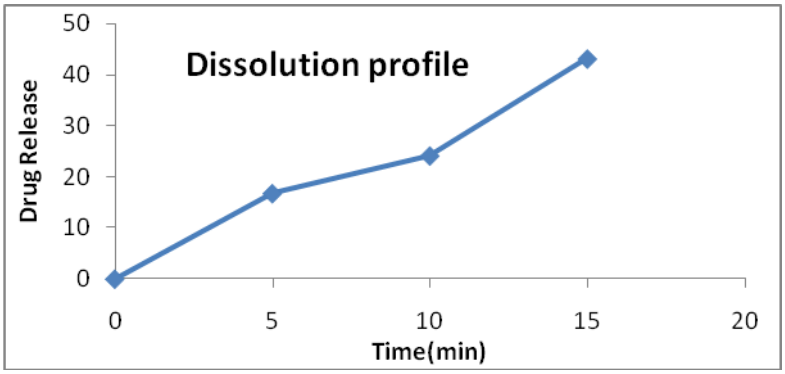

Figure -21:–Drug Release Profile of Telmisartan pure drug.

Table -10:- Drug Release of formulations F1- F9 and Pure Drug.

Time(min)	Pure Drug	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0	0
5	16.75	50.45	58.50	66.61	44.60	47.73	49.08	45.70	50.81	63.14
10	24.12	75.06	78.58	87.74	66.71	69.07	72.48	69.45	72.53	78.76
15	43.12	91.16	93.37	94.42	86.44	87.57	90.48	88.39	92.48	97.74

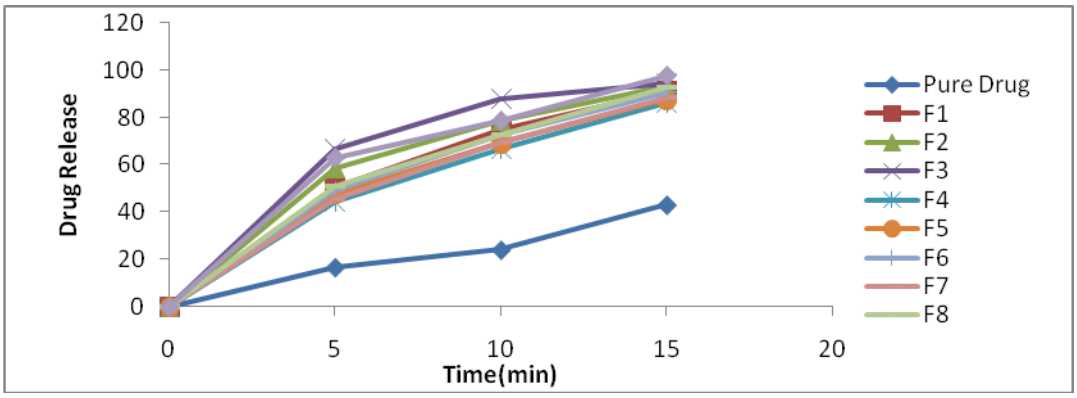

Figure -22:-Comparative Studies of % DR of Pure drug with formulations F1 to F 9.

ISSN PRINT 2319 1775 Online 2320 7876

Research paper UGC CARE Listed (Group -I) Journal Volume 11,S Iss 3, Dec 2022

Table-11: - R^2 -values of different formulations.

FORMULATIONS	ZERO ORDER	FIRST ORDER
F1	0.934	0.989
F2	0.894	0.987
F3	0.858	0.952
F4	0.957	0.983
F5	0.943	0.987
F6	0.939	0.983
F7	0.955	0.983
F8	0.942	0.944
F9	0.885	0.920

CONCLUSION

All of the prepared solid dispersions were discovered to be smooth and free flowing. The prepared solid dispersions' estimated drug content was determined to be uniform. Increased dissolution rates were observed with all the solid dispersions when compared to pure drug. The rank order of increment in dissolution rate was observed with β-CD > PEG 6000 > Pure Drug. The concentration of the medication to carrier ratio has a significant impact on the pace of telmisartan dissolution. The 1:5 ratio (Drug: -CD) showed the greatest improvement in telmisartan's rate of dissolution among the several solid mixes produced.From DSC, FTIR study we concluded that the drug was compatible with all of the selected excipients. From XRD study we found that the drug is in amorphous form in solid dispersion so more soluble.

FUNDING RESOURCES

Declared None

ACKNOWLEDGEMENT

The authors acknowledge the contribution of Centurion University of Technology and Management,Odisha, India, University Department of Pharmaceutical Sciences, Utkal University,VaniVihar, Bhubaneswar, Odisha, India and Roland Institute of Pharmaceutical Sciences,Berhampur, Odisha, India for their valuable contribution to carry out this research work.

CONFLICT OF INTEREST

Declared None

REFERENCES:

1. Eswaraiah MC, Jaya S. Enhancement of dissolution rate of telmisartan by solid dispersion technique. Res J Pharm Technol. 2020;13(5):2217-20. doi: HYPERLINK "https://doi.org/10.5958/0974-360x.2020.00398.4" \t "_blank" 10.5958/0974-360X.2020.00398.4 .
2. Mandake GR, Shinde SS, Patil OA, Nitalikar MM. Dissolution enhancement of telmisartan by spray drying technique. Asian J Pharm Technol. 2018;8(4):264. doi: HYPERLINK "https://doi.org/10.5958/2231-5713.2018.00041.7" \t "_blank" 10.5958/2231-5713.2018.00041.7 .

ISSN PRINT 2319 1775 Online 2320 7876

Research paper UGC CARE Listed (Group -I) Journal Volume 11,S Iss 3, Dec 2022

3. Paul AD, Vinay J, Rajyalakshmi KG, Prasad PV. Formulation design for poorly water-soluble drug by using solid dispersion of telmisartan for solubility and dissolution rate enhancement. Vol. 7(4); 2019. doi: HYPERLINK "https://doi.org/10.19080/gjpps.2019.07.555716" \t "_blank" 10.19080/GJPPS.2019.07.555716 .
4. Singh G, Kaur L, Gupta GD, Sharma S. Enhancement of the solubility of poorly water soluble drugs through solid dispersion: A comprehensive review. Indian J Pharm Sci (Vol. 79, Issue 5, pp. 674–687) . Increasing dissolution rate of telmisartan tablet by dispersion method . 2017. doi: HYPERLINK "https://doi.org/10.4172/pharmaceutical-sciences.1000279" \t "_blank" 10.4172/PHARMACEUTICAL-SCIENCES.1000279 .
5. Supriya A, Manasa B, Shilpa T, Kaza R, Savithramma S, Prasadu D. Dissolution improvement of telmisartan by surface solid dispersion method. Acta Sci Pharm Sci. 2018;2(1):24-8.
6. Kundu S, Kumari N, Soni SR, Ranjan S, Kumar R, Sharon A *et al*. Enhanced solubility of telmisartan phthalic acid cocrystals within the pH range of a systemic absorption site. ACS Omega. 2018;3(11):15380-8. doi: HYPERLINK "https://doi.org/10.1021/acsomega.8b02144" \t "_blank" 10.1021/acsomega.8b02144 , PMID HYPERLINK "https://www.ncbi.nlm.nih.gov/pubmed/31458196" \t "_blank" 31458196 .
7. AlKhalidi MM, J. Jawad F. Enhancement of aqueous solubility and dissolution rate of etoricoxib by solid dispersion technique. Iraqi J Pharm Sci. 2020;29(1):76-87. doi: HYPERLINK "https://doi.org/10.31351/vol29iss1pp76-87" \t "_blank" 10.31351/VOL29ISS1PP76-87 .
8. Dubey A, Nagar T. Road, R, and Pradesh, M. Enhancement of Aqueous Solubility and Diss of Telmisartan. 2014;5(10):4478-85. doi: HYPERLINK "https://doi.org/10.13040/ijpsr.0975-8232.5(10).4478-85" \t "_blank" 10.13040/IJPSR.0975-8232.5(10).4478-85 .
9. Putta SK, P, P. S.S. Enhanced solubility and dissolution rate of telmisartan by quasi emulsion solvent diffusion and spherical agglomeration techniques: A comparative study. J Chem Pharm Sci. 2017;10(1):203-10.
10. Bhise S, Mathure D, Patil MV, Patankar RD. Solubility enhancement of antihypertensive agent by solid dispersion technique. Int J Pharm Life Sci (IJPLS). 2011;2(8):970-5.
11. Patel H, Patel H, Gohel M, Tiwari S. Dissolution rate improvement of telmisartan through modified MCC pellets using 32 full factorial design. Saudi Pharm J. 2016;24(5):579-87. doi: HYPERLINK "https://doi.org/10.1016/j.jsps.2015.03.007" \t "_blank" 10.1016/j.jsps.2015.03.007 , PMID HYPERLINK "https://www.ncbi.nlm.nih.gov/pubmed/27752231" \t "_blank" 27752231 .
12. Kothawade SN, Kadam NR, Aragade PD, Baheti DG. Formulation and characterization of telmisatan solid dispersions. Int J PharmTech Res. 2010;2(1):341-7.
13. Wienen W, Entzeroth M, Meel JCA, Stangier J, Busch U, Ebner T *et al*. A Review on Telmisartan: A Novel, Long-Acting Angiotensin II-Receptor Antagonist. Cardiovasc Drug Rev. 2000;18(2):127-54. doi: HYPERLINK

ISSN PRINT 2319 1775 Online 2320 7876

Research paper UGC CARE Listed (Group -I) Journal Volume 11,S Iss 3, Dec 2022

"https://doi.org/10.1111/j.1527-3466.2000.tb00039.x" \t "_blank" 10.1111/j.1527-3466.2000.tb00039.x .

14. Bhowmik D, Jayakar B, Sampath Kumar K. Design and characterization of fast dissolving tablet of telmisartan. Int J Pharma Recent Research. 2009;1(1):31-40.
15. Patil M, Keny R, Mandlik S, Saindane D, Gaikwad D, Khade T. Characterization and formulation of solid dispersion of telmisartan using $NaHCO_3$by Hot Melt method. IJPI's Journal of Pharmaceutics and Cosmetology. 2011;1(3):20-33.
16. Patil M, Keny R, Mandlik S, Saindane D, Gaikwad D, Khade T. Formulation and evaluation of solid dispersion of telmisartan with KOH as alkalizer by hot melt method. J Pharm Biomedical Sci. 2010;1(16):1-7.
17. Patel B, Parikh RH, Swarnkar D. Enhancement of dissolution of telmisartan through use of solid dispersion technique - surface solid dispersion. J Pharm Bioallied Sci. 2012 Mar;4(Suppl 1);Suppl 1:S64-8. doi: HYPERLINK "https://doi.org/10.4103/0975-7406.94142" \t "_blank" 10.4103/0975-7406.94142 , PMID HYPERLINK "http://www.ncbi.nlm.nih.gov/pubmed/23066211" \t "_blank" 23066211 , PMCID HYPERLINK "https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3467836" \t "_blank" PMC3467836 .
18. Nisha, Behera, Kumar A. Vyas, Maulesh and Jaiswal, Arpita and Upadhyay. 2014. Formulation and development of solubility improvised complex of telmisartan using various techniques. International journal of universal pharmacy and bio sciences;3:311-26.
19. Kausalya, J and Suresh, K and Padmapriya, S and Rupenagunta, Anusha and Senthilnathan, B. 2010. Solubility and Dissolution Enhancement Profile of telmisartan using various techniques. Int J Pharm Tech Res.3. 1737-49.
20. Parikh BN. Formulation, Optimization and Evaluation of Immediate release Tablet of telmisartan. J Glob Pharm Technol. 2010;2:79-84
21. Kundu, S, Kumari, N, Soni, SR, Ranjan, S, Kumar, R, Sharon A, Ghosh A. 2018. Enhanced Solubility of Telmisartan Phthalic Acid Cocrystals within the pH Range of a Systemic Absorption Site.. ACS Omega .3 (11).15380-15388.doi: https://doi.org/10.1021/acsomega.8b02144