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# FORMULATION AND EVALUATION OF SOLUBILITY ENHANCED MOUTH DISSOLVING FILM OF TELMISARTAN

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## ABSTRACT
Telmisartan is BCS Class II drug hence it need to increase its solubility. The present study describes preparation and characterization Solid Dispersion incorporated mouth dissolving film of Telmisartan. By Preparation of solid Dispersion through kneading method Followed by Solvent Casting Method to formulate the MDF. Solid Dispersion is evaluated for Solubility, drug content and drug release rate for screening of Carrier for further formulation. The in-vitro drug release study demonstrated that enhanced the solubility and Rapid drug Release from Solid Dispersion than pure drug. The prepare films were evaluated for their physicochemical and mechanical parameter such as Physical appearance, surface PH, Thickness uniformity, Disintegration time, Drug content uniformity, folding endurance, and In-vitro drug release. The method was optimized by applying 32 level factorial designs. The effects of composition of Film forming polymer and Super disintegration on Appearance of film, disintegrating time, and in-vitro drug release behaviour were investigated the in-vitro Drug Release and Disintegration time of optimized formulation (F7) was found to be 91.83 %, and 29 sec respectively. This optimized batch was studied for its stability for 1 month.

**KEYWORD:** Telmisartan, Solid Dispersion, Mouth Dissolving Film, Optimized Batch.

## INTRODUCTION
Solid dispersion technology is the science of dispersing one or more active ingredients in an inert matrix in the solid stage to achieve an increased dissolution rate or sustained release of drug, altered solid state properties and improved stability. The term solid dispersion refers to a group of solid products consisting of at least two different components, generally a hydrophilic matrix and a hydrophobic drug. The matrix can be either crystalline or amorphous. The drug can be dispersed molecularly, in amorphous particles (clusters) or in crystalline particles.[3] Kneading Technique this method, carrier is permeated with water and transformed to paste. Drug is then added and kneaded for particular time. The kneaded mixture is then dried and passed through sieve if necessary.

Oral Fast Dissolving Films (FDF) are also known as Mouth dissolving films (MDF), oral strips, Orodispersible films (ODF). On placing mouth dissolving films in the mouth, saliva serves to rapidly dissolve the dosage form. The saliva containing the dissolved or dispersed medicament is then swallowed and the drug is absorbed in the normal way. Some drugs are absorbed from the mouth, pharynx and oesophagus as the saliva passes down into the stomach & it may produce rapid onset of action. In such cases bioavailability of drug is significantly greater than those observed from conventional tablets dosage form.[1,2,3]

Mouth dissolving drug delivery system (MD-DDS) offers better absorption of certain drugs through Oral mucosa which gives direct entry of such active pharmaceutical ingredient into the systemic circulation. This is useful to increase the bioavailability of drug which undergoes first pass hepatic metabolism and gastrointestinal degradation. The approach used in the present investigation for delivery of drug is by buccal route to increase the bioavailability of drug, by avoiding first pass metabolism as well as to provide advantages like easy accessibility, patient compliance and rapid drug action to control the Hypertension. Following local stress and ability to withstand environmental extremes like change in pH, temperature etc. Telmisartan is an antihypertensive drug with oral bioavailability of 45-48% due to first pass metabolism. In this study an attempt would be made to develop an efficient single dosage form for delivery of Telmisartan in the form of mouth dissolving film to avoid its hepatic or presystemic metabolism and to produce rapid onset of action. Also the aim of this work is to increase the solubility of Telmisartan by formulating Solid Dispersion of Telmisartan with different Carrier. And also study the effect of various polymers and plasticizer in different

concentrations on physical, mechanical and performance properties of the film.

**Objectives of the present investigation was**

1. To enhanced the solubility of Telmisartan by formulating the solid dispersion.
2. To evaluate the effect of different polymer on solubility of Telmisartan.
3. To formulate and in-vitro evaluate Solid Dispersion incorporated Mouth dissolving films of Telmisartan.

## MATERIAL AND METHOD

Telmisartan (VS International pvt ltd), HPMC E15(VS international pvt ltd.), Beta-cyclodextrin (Purchase from Modern Lab, Nashik), Sodium starch Glycol (Merck Ltd), Propylene Glycol (Modern lab,Nashik), Citric acid (FMC Biopolymer), Sucralose (Nutrasweet).

### Method

**1] Solid Dispersion is formulated by kneading method:-** Weight accurately Drug and Carriers in 1:1 ratio. Transfer into Mortar and Grinding continuously. Then add drop by drop Methanol: water (1:1) and Grind for 30-45 mint. Thick past mass is form, dry into oven. Pass from the Sieve and Store for Further evaluation.

**2] Preparation of Oral fast dissolving films**

The Fast dissolving films were prepared by solvent casting technique. Various polymers were used as a film forming polymer. Accurately weighed quantity of polymer was dissolved in specified quantity of water. Weighed quantity of plasticizer was added to the above solution and dissolved by using magnetic stirrer. Weighed quantity of Telmisartan Solid Dispersion was dissolved in 2 ml of appropriate solvent, separately. Solution of Telmisartan Solid Dispersion was added to previously prepared solution of polymer and plasticizer, and mixed thoroughly. The above solution kept a side for 10 minute for removal of air bubbles, or may kept for sonication if required. Then casted on petri plate and dried to overnight to form the film. Then the film was carefully removed and cut into suitable size i.e. 2cm x 2cm. Solution of Telmisartan Solid Dispersion was added to previously prepared solution of polymer and plasticizer, and mixed thoroughly Solution of Telmisartan Solid Dispersion was added to previously prepared solution of polymer and plasticizer, and mixed thoroughly. The above solution kept a side for 10 minute for removal of air bubbles, or may kept for sonication if required. Then casted on petri plate and dried to overnight to form the film. Then the film was carefully removed and cut into suitable size i.e. 2cm x 2cm.

## RESULT AND DISCUSSION

### 1] Evaluation of solid dispersion of Telmisartan

**1. ATR spectra of Solid Dispersion**

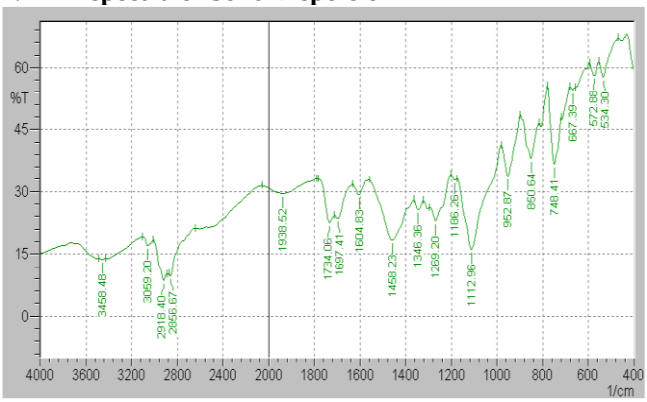


**Fig No.1: FTIR Spectra of Telmisartan Solid Dispersion physical mixture.**

**2. DSC Thermo-gram of solid dispersion**

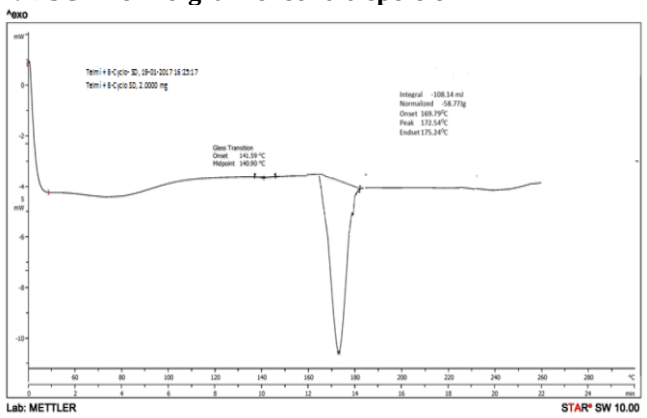


**Fig. No. 2: DSC of Thermogram of Telmisartan Solid Dispersion physical mixture.**

**3. Solubility of Solid Dispersion**

Solubility. For the determination of solubility, excess amount of Solid Dispersion was added in the solvent (water, 6.8 pH phosphate buffer) at room temperature and kept for 48hrs with occasional shaking. The supernatant was taken and analyzed by using Shimadzu UV 2450 double beam spectrophotometer. Dilute the sample if needed. (100 fold or 1000 fold).

**Table. No.1: Solubility of Telmisartan Solid Dispersion in Various Solvent**

| Sr. No | Formulation | Water | Phosphate Buffer PH6.8 |
|---|---|---|---|
| 1 | Telmi + Beta-cyclodextrin | 2.576 | 2.98 |
| 2 | Telmi + Gelucire | 1.84 | 2.62 |
| 3 | Telmi + Solu-plus | 1.415 | 1.899 |

**4. Evaluation of Drug Content:** Percent Drug content in Telmisartan Solid Dispersion. . Equivalent to 10mg Drug Solid Dispersion was dissolve in 10 ml of methanol. Filter and filtrate is evaluate for Drug Content by UV. Dilution is done using methanol. Drug Content is

Calculate using following formulation. Percent Drug Content is calculated by UV Analysis Method.

**Table No.2. Percent Drug Content Telmisartan Solid Dispersion.**

| Sr. No. | Formulation | % Drug Content |
|---|---|---|
| 1 | Telmi + Beta-cyclodextrin | 98.86 |
| 2 | Telmi + Gelucire | 97.22 |
| 3 | Telmi + Solu-plus | 94.30 |
| 4 | Telmi + PEG 6000 | 97.15 |
| 5 | Telmi + PVP | 96.01 |

**5. Percent drug release from Solid dispersion**

Percent drug release Rate from Telmisartan Solid Dispersion. Percent Drug Release is determined using USP Apparatus I (Basket) Procedure. Take 900ml of Phosphate Buffer PH 6.8 in each vessel. Take 40mg Drug and Solid Dispersion Equivalent to 40mg drug. Place each sample in Basket (Wrapped the sample in Muslin cloth). Maintain the temp 370c and Basket speed 50rpm. Withdraw the 10 ml sample after interval time and analysed for percent Drug Release using UV Spectroscopy. The medium use for dissolution is Phosphate buffer PH 6.8 (900ml) at 50 RPM at temperature 37ºC +_ 0.5.

**Table No. 3. Drug Release from plain Telmisartan and Telmisartan Solid Dispersion.**

| Formulation | % Drug Release (at 60 mint) |
|---|---|
| Telmisartan | 41.79 |
| Telmi+ Beta cyclo | 71.08 |
| Telmi+ Gelucire | 60.98 |
| Telmi+ solu-plus | 57.8 |
| Telmi+PEG6000 | 56.46 |
| Telmi+PVP | 53.03 |

**2] Formulation and evaluation of oral fast dissolving film**

**1] Dose Calculation**

Diameter of the Petri plate: 9.2 cm.

Area of the plate: 66.44 cm2.

No. of 4 cm2 films presented in whole plate: 16.61 no. of films Each film containing 4 mg of Telmisartan. So, 16 no. of films will contain 64 mg of Telmisartan. The amount of Telmisartan to be loaded = 64 mg.

**2] Role of casting surface:** The films cast in the Petri plates showed better films forming capacity, appearance than the films cast in the plastic plates. Films were easy to remove from the Petri plates.

**3] Trial Batches of Polymers Screening for Preparation of Film.:** Appearance of films of PVP K30 and PVA were found to be good film forming capacity but semi-transparent and their texture was found to be rough. HPMC E 15 shows the desirable film forming capacity and appearance as transparent. Hence HPMC E 15 was selected for further study.

**Table. 4: Screening of Polymer for Preparation of Film.**

| Sr. Code | Polymer Used | Film Forming | Appearance |
|---|---|---|---|
| P1 | Chitosan | Good | Semi-transparent, Glassy |
| P2 | PVA | Good | Semi-transparent, Glassy |
| P3 | HPMC | Excellence | Transparent |

**4] Trials of Plasticizer Screening for Preparation of Film:** S1 to S6 formulations were prepared using HPMC polymers using different plasticizer such as glycerol and Propylene glycol. All these films were evaluated for appearance, disintegration time and Folding endurance.

**Table No. 5: Screening of Plasticizer for Preparation of Film.**

| Formulation Code | Appearance | Disintegration time (sec.) | Folding Endurance |
|---|---|---|---|
| SL 1 | Transparent | 57 | 143 |
| SL 2 | Transparent | 50 | 156 |
| SL 3 | Transparent | 49 | 151 |
| SL 4 | Transparent, sticky | 61 | 110 |
| SL 5 | Transparent, sticky | 57 | 122 |
| SL 6 | Transparent, sticky | 52 | 108 |

All formulation were evaluated on the basis of their disintegration time and folding endurance.

All formulation were observed as transparent in nature and the film formulated by Glycerine as very sticky in nature. The propylene glycol was used in S3 formulation at 0.6 ml v/w concentration and it shows less disintegration time and good folding endurance as compared to formulations were prepared by propylene glycol and Glycerol at different concentration used as plasticizer. Hence the propylene glycol used as the plasticizer at 0.6 ml v/w concentration in further formulation.

**5] Optimization of Formulation:** A 32 randomized full factorial design was used in the present study. In this design 2 factors were evaluated each at 3 levels, and experimental trials were performed at all 9 possible combinations. *In vitro* disintegration time (DT) and percent cumulative drug release (%CDR) in 5 min were

selected as dependent variables. Two independent factors, the concentration of HPMC (X1), SSG (X2) were set at three levels ; Low, Medium and High levels of each factor were coded as - 1, 0 and +1, respectively shown in table.no.6.

**Table No.6: Independent Variable.**

| Formulation Factors, Concentrations and Levels. | HPMC E 15 (X1) | | | SSG (X2) | | |
|---|---|---|---|---|---|---|
| Concentration (mg) | 600 | 650 | 700 | 8 | 12 | 16 |
| Levels | -1 | 0 | 1 | -1 | 0 | 1 |

**Evaluation of all films formulation**

**Table No.7: Evaluation parameters of all formulation (F1-F9).**

| Formulation Code | Weight(mg) | Thickness(mm) | Surface pH | Folding Endurance | Drug Content |
|---|---|---|---|---|---|
| F1 | 120.27 | 0.53 | 6.3 | 145 | 91.45 |
| F2 | 129.63 | 0.45 | 6.3 | 149 | 90.88 |
| F3 | 135.17 | 0.56 | 6.4 | 158 | 95.72 |
| F4 | 128.13 | 0.45 | 6.4 | 142 | 92.87 |
| F5 | 133.53 | 0.46 | 6.6 | 145 | 92.59 |
| F6 | 136.52 | 0.67 | 6.5 | 155 | 95.44 |
| F7 | 132.20 | 0.45 | 6.6 | 141 | 93.77 |
| F8 | 137.47 | 0.49 | 6.2 | 143 | 64.36 |
| F9 | 142.53 | 0.45 | 6.8 | 152 | 96.58 |

**Dissolution study**

**Table No. 8: Dissolution data of F1 to F9 formulation.**

| Formulation Code | Cumulative %drug Release from F1 to F9 | | | | | |
|---|---|---|---|---|---|---|
| | 0.5 | 1 | 2 | 3 | 4 | 5 |
| F1 | 22.52 | 43.95 | 60.47 | 75.00 | 82.74 | 88.27 |
| F2 | 17.97 | 37.72 | 59.02 | 71.68 | 82.84 | |
| F3 | 18.70 | 37.29 | 59.91 | 70.68 | 78.73 | |
| F4 | 26.05 | 42.37 | 61.81 | 72.49 | 87.87 | |
| F5 | 20.91 | 39.08 | 60.89 | 71.86 | 82.86 | |
| F6 | 26.61 | 38.05 | 60.53 | 73.32 | 82.72 | |
| F7 | 25.76 | 43.25 | 61.82 | 73.09 | 88.47 | |
| F8 | 18.70 | 38.32 | 55.92 | 71.46 | 83.08 | |
| F9 | 23.41 | 41.31 | 60.59 | 73.06 | 83.57 | |

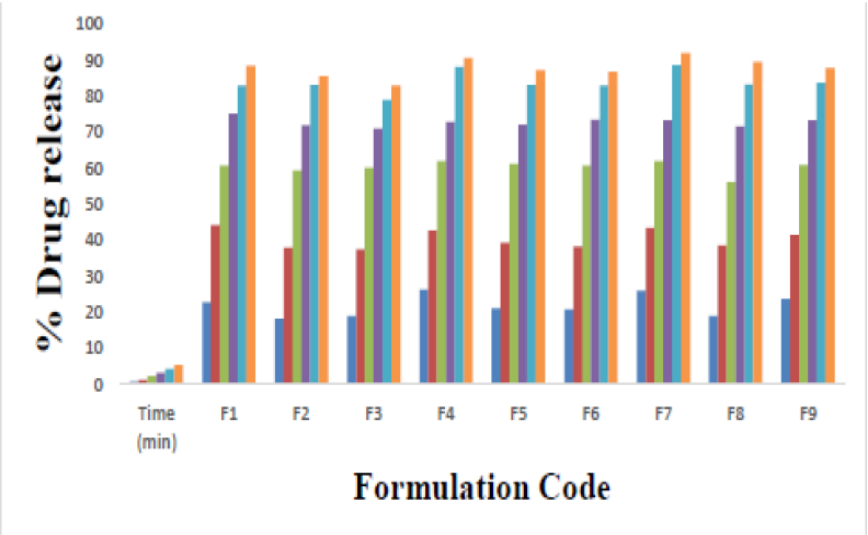


**Fig No. 3: Dissolution data of F1 to F9 formulation.**

**Table No.9: Actual Factorial Response Design.**

| Formulation Code | Factor 1 A:HPMC Mg | Factor 2 B:SSG Mg | Response 1 %Drug Release % DR | Response 2 Disintegration Sec |
|---|---|---|---|---|
| F1 | 600 | 8 | 88.27 | 46 |
| F2 | 650 | 8 | 85.29 | 51 |
| F3 | 700 | 8 | 82.75 | 56 |
| F4 | 600 | 12 | 90.36 | 34 |
| F5 | 650 | 12 | 87.03 | 40 |
| F6 | 700 | 12 | 86.52 | 45 |
| F7 | 600 | 16 | 91.83 | 29 |
| F8 | 650 | 16 | 89.21 | 35 |
| F9 | 700 | 16 | 87.48 | 40 |

**3] Stability Study**

**Table No.10: Stability Study.**

| Smpling Time Interval (Days) | Weight (mg) | Folding Endorance | Surface PH | Drug Content Uniformity (%) | Disintegration Time(sec) |
|---|---|---|---|---|---|
| **Initial** | 132.20 | 141 | 6.6 | 93.77 | 29 |
| 15 | 131.18 | 138 | 6.6 | 93.41 | 32 |
| 30 | 131.12 | 140 | 6.5 | 93.19 | 32 |

## CONCLUSION

Films of HPMC E15 and SSG showed the desired film forming characteristics, cumulative % drug release & Disintegration.Effect of HPMC E15 and SSG on cumulative drug release and disintegration time of film was compared. Films of F7 formulation showed slightly higher cumulative % drug release and lower disintegration time than films of other formulations. hence HPMC E15 and SSG film was selected for optimization of formulation. So, formulation was optimized using 32 full factorial design. Formulation F7 showed slightly higher cumulative % drug release and lower disintegration time and desired physical evaluation parameters. So, the formulation F7 containing, 600 mg of HPMC E15 and 16 mg of SSG was considered to be the optimized formulation. It was found that as concentration of HPMC E15 in formulation was increased, cumulative % drug release decrease and increase in concentration of SSG, increase % drug release from the formulation significantly. It can be concluded that mouth dissolving film of Telmisartan can be formulated using HPMC E15 as a film forming polymer and SSG as a superdisintegrant. Hence, Telmisartan can be conveniently administered orally in the form of films.

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