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Formulation, Optimization and Evaluation of Immediate Release Tablet of Telmisartan

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Abstract In the present investigation an attempt was made to develop solid oral formulations of Telmisartan which can be prepared using less complicated and expensive processes and fulfill all prerequisites for pharmaceutical use, i.e. long-lasting stability of the formulation under different climatic conditions and sufficient solubility of the active substance for sufficient gastrointestinal absorption in the slightly acidic and neutral pH region. Preferably, the formulations should have immediate release characteristics and a dissolution showing no essential pH dependency within the physiological relevant pH interval of the gastrointestinal tract. Tablets were evaluated for various parameters like, weight variation, content uniformity, in-vitro dissolution studies were performed using United States Pharmacopeia (USP) apparatus type II. The effects of concentration of meglumine, povidone and different alkalizers on the release rate of Telmisartan were studied. Telmisartan has poor and pH dependent water solubility in order to enhance its dissolution different alkalizers were used. Thus significantly increased the drug dissolution rate in intestinal stimulated fluid (pH 7.5), slightly acidic (pH 1.2) and water.

Keywords Telmisartan, wet granulation, *in vitro* dissolution

Introduction

Tablets are solid preparations each containing a single dose of one or more active substances and usually obtained by compressing uniform volumes of particles. Tablets are intended for oral administration. Some are swallowed whole, some after being chewed, some are dissolved or dispersed in water before being administered and some are retained in the mouth where the active substance is liberated.

Introduction to Immediate Release Dosage Form [11,12]

These are designed for immediate release of drug for rapid absorption. Disintegrating agents are substances routinely included in tablet formulations and in some hard-shell capsule formulations to promote moisture penetration and dispersion of the matrix of the dosage form in dissolution fluids. Super disintegrants improve disintegrant efficiency resulting in decreased use levels when compared to traditional disintegrants.

Mechanism of Disintegrants:

High swellability
Capillary action and high swellability
Chemical reaction

When introduced to an aqueous environment of use, the tablet rapidly takes up water, leading to swelling of the disintegrant and rapid disintegration of the tablet before the dispersion polymer can form a hydrogel. The disintegrant should be chosen such that it

1. swells rapidly when introduced into the use environment and
2. has a low tendency to form or promote formation of a hydrogel.

The rate of swelling of the disintegrant is directly correlated to tablet disintegration times. Tablets containing disintegrants cause more rapid swelling have faster disintegration times at comparable disintegrant levels.

Composition of Immediate Release Dosage Form [12]

The immediate release dosage form comprises the dispersion, a porosigen, and a disintegrant. The dosage form is in the form of a compressed tablet or other solid dosage form. Other conventional formulation excipients may be employed in the dosage forms including surfactants, pH modifiers, fillers, matrix materials, complexing agents, solubilizers, pigments, lubricants, glidants, flavorants, may be used for customary purposes and in typical amounts without adversely affecting the properties of the compositions.

Solid Dispersion

The dosage forms contain a high loading of the solid amorphous dispersion. High loadings of dispersion in the dosage form minimize the size of the dosage form, making it easier for the patient to swallow it and improving patient compliance. Depending on the drug dose, the immediate release dosage form comprises at least 30-50 wt % of the dispersion.

Concentration-Enhancing Polymers

Concentration-enhancing polymers suitable for use in the solid drug dispersions in the sense that they do not chemically react with the drug in an adverse manner. The polymer can be neutral or ionizable, and should have an aqueous solubility of at least 0.1 mg/mL over at least a portion of the pH range of 1-8.

Preparation of Dispersions

Different methods are also been used for preparation of solid dispersions such as Melting method, Solvent method, melting solvent method (melt evaporation), Melt extrusion method, Lyophilisation Technique, Melt Agglomeration Process, The Use of Surfactant, Electrospinning and Super Critical Fluid Technology.

Disintegrants

As disintegrants sodium starch glycolate, sodium carboxymethyl cellulose, calcium carboxymethyl cellulose, croscarmellose sodium, crospovidone, polyvinyl polypyrrolidone, methyl cellulose, microcrystalline cellulose, powdered cellulose, lower alkyl-substituted hydroxypropyl cellulose, polacrilin potassium, starch, pregelatinized starch, sodium alginate, and mixtures thereof. The amount of disintegrant included in the dosage form will depend on several factors.

Porosigen

The dosage form also includes a porosigen. A "porosigen" is a material that, when present in the formulation containing the solid amorphous dispersion, leads to a high porosity and high strength following compression of the blend into a tablet. In addition, preferred porosigens are soluble in an acidic environment with aqueous solubilities typically greater than 1 mg/mL at a pH less than about 5.

Surfactants

One very useful class of excipients is surfactants, preferably present from 0 to 10 wt %. Suitable surfactants include fatty acid and alkyl sulfonates; commercial surfactants such as benzalkonium chloride, dioctyl sodium

sulfosuccinate, polyoxyethylene sorbitan fatty acid esters, natural surfactants such as sodium taurocholic acid, lecithin, and other phospholipids and mono- and diglycerides; and mixtures thereof.

pH Modifiers

Inclusion of pH modifiers such as acids, bases, or buffers may also be beneficial in an amount of from 0 to 10 wt %. Acidic pH modifiers (e.g., acids such as citric acid or succinic acid) retard the dissolution of the pharmaceutical composition when the dispersion polymer is anionic. Alternatively, basic pH modifiers (e.g., sodium acetate or amines) enhance the rate of dissolution of the same types of pharmaceutical composition.

Diluents

Examples of other matrix materials, fillers, or diluents include lactose, mannitol, xylitol, dextrose, sucrose, sorbitol, compressible sugar, microcrystalline cellulose, powdered cellulose, starch, pregelatinized starch, dextrates, dextran, dextrin, dextrose, maltodextrin, calcium carbonate, dibasic calcium phosphate, tribasic calcium phosphate, calcium sulfate, magnesium carbonate, magnesium oxide, poloxamers, polyethylene oxide, hydroxypropyl methyl cellulose and mixtures thereof.

Surface Active Agents

Sodium lauryl sulfate and polysorbate 80.

Drug-complexing agents or solubilizers include the polyethylene glycols, caffeine, xanthene, gentisic acid and cylodextrins.

Lubricants

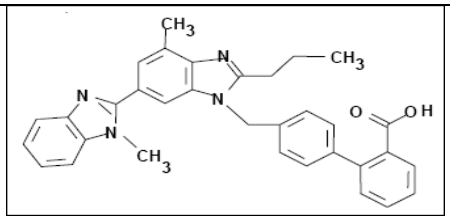
Examples of lubricants include calcium stearate, glyceryl monostearate, glyceryl palmitostearate, hydrogenated vegetable oil, light mineral oil, magnesium stearate, mineral oil, polyethylene glycol, sodium benzoate, sodium lauryl sulfate, sodium stearyl fumarate, stearic acid, talc and zinc stearate.

Glidants

Examples of glidants include silicon dioxide, talc and cornstarch.

Introduction to Drug[17]

Table 1: Drug Profile

Sr. No.	Parameter	Description
1	Chemical structure	
2	Chemical Name	4'-[(1,4'-dimethyl-2'-propyl [2,6'-bi-1H-benzimidazol]-1'- yl)methyl]-[1,1'-biphenyl]-2-carboxylic acid
3	Appearance	White to slightly yellowish solid
4	Molecular formula	C33H30N4O2
5	Molecular weight	514.63g/mol
6	Category	It is a nonpeptide angiotensin II receptor (type AT1) antagonist (Angiotensin Receptor Blocker- ARB) used in

		the management of hypertension
7	BCS class	Class II
8	Solubility	It is practically insoluble in water and in the pH range of 3 to 9, sparingly soluble in strong acid (except insoluble in hydrochloric acid), and soluble in strong base.
9	Melting Point	261-263ºC
10	Daily Dose	40-80 mg

Hypertension, commonly referred to as "high blood pressure", is a medical condition where the pressure is chronically elevated is one of the commonly found diseases, affecting most of the populations in the world. For treating hypertension, commonly used drugs include ACE inhibitors, Alpha Blockers, Beta Blockers, Angiotensin receptor Blockers, Calcium Channel Blocker, Diuretics and combination of any of these categories.

Material & Method

Materials used in the Present Investigation

Table 2: Materials Used in the Present Investigation

Sr. No.	Materials	Description
1.	Telmisartan	Alembic research centre, Baroda
2.	Sorbitol	FMC Biopolymer, Shanghai, China
3.	Povidone (PVP K 25)	Xine medicine Health Product Company, China
4.	Sodium Hydroxide	Dow Chemicals, India
5.	Meglumine	Green Fine Chemical Co., Ltd. Shangai, China
6.	Sodium Starch Glycolate	FMC Biopolymer, Shanghai, China
7.	Magnesium Stearate	Mallinckrodt Chemicals

Equipments Used in the Present Investigation

Table 3: Equipments/Machines Used in the Present Investigation

Sr. No.	Instruments	Make	Model
1	Stirrer	Remi Motors Ltd.	RQ-124A
2	Rapid Mixer and Wet Granulator	Saral Engineering Company	RMG 25.7.5.0
3	Fluid bed Dryer	Global Engineering	TG-400
4	Sieves	Atlanto enterprise	**
5	Multimill	Shakti Engineering	Mini Multi Mill
6	Conta Blender	Gansons	GMP
7	Tap Density Tester (USP)	Electrolab	ETD-1020
8.	Halogen Moisture Analyser	Mettler-Toledo	HR73
9	Rotary Tablet Machine	Rimek	12 station
10	Electronic Vernier Calipers	**	**
11	Tablet Hardness Tester	Pharmatron	Dr.Schleuniger 8M
12	Friabilator (USP)	Electrolab	EF-1W
13	Disintegration Tester (USP)	Electrolab	ED-2L
14	Tablet Dissolution Tester(USP Type II)	Electrolab	TDT-06P

15	UV-Visible Spectrophotometer	Shimadzu	Pharmaspec UV-1700

Preformulation Study [94]

The objective of preformulation studies are to develop a portfolio of information about the drug substance, so that this information useful to develop formulation. Preformulation can be defined as investigation of physical and chemical properties of drug substance alone and when combined with excipients.

Organoleptic Characteristics

Table 4: Organoleptic Characteristics of API

Properties	Results
Description	Powder
Taste	Highly bitter
Odor	Odorless
Color	White

Solubility of Drug [95]

The solubility of Telmisartan was determined in simulated gastric fluid (pH 1.2) prepared by dissolving NaCl in deionized water and adjusted by 7.4% HCl solution, simulated intestinal fluid (pH 7.5) prepared by dissolving KH_2PO_4 in deionized water and adjusted by NaOH 1 N solution, distilled water and in a 1% w/v solution of the pH modifiers like NaOH by adding an excess amount of Telmisartan to snap-cap Eppendorf tube containing 1 mL of media. 10 mg of Telmisartan was added except for NaOH solution about 130 mg of Telmisartan was added gradually due to significantly high solubility in alkalizers' solution. The resulting mixture was thoroughly vortexed and then placed in a 37 °C incubator for two days. Aliquots were centrifuged at 1000 rpm for 10 min. The supernatant layer was carefully removed and then diluted with a solution. The concentration of Telmisartan was then measured using HPLC by comparison with a standard calibration curve.

Table 5: Solubility of Telmisartan at 37 °C in Different Media

Sr No.	Media	Solubility (µg/mL)
1	Distilled water	0.094
2	Gastric fluid (pH 1.2)	510.55±6.77
3	Intestinal fluid (pH 7.5)	0.26±0.04
4	NaOH	1.28×10^5±3.47

Determination of Bulk Density

The ratio of mass to volume is known as density.

Apparent Bulk Density

Weigh accurately 25 g of drug (M), which was previously passed through 20# sieve and transferred in 100 ml graduated cylinder. Carefully level the powder without compacting, and read the unsettled apparent volume (V_0). Calculate the apparent bulk density in gm/ml by the following formula:

Bulk density = Weight of powder / Bulk volume

Tapped Density

Weigh accurately 25 g of drug, which was previously passed through 20# sieve and transfer in 100 ml graduated cylinder. Then mechanically tap the cylinder containing the sample by raising the cylinder and allowing it to drop under its own weight using mechanical tapped density tester that provides a fixed drop of 14 ± 2 mm at a nominal rate of 300 drops per minute. Tap the cylinder for 500 times initially and measure the tapped volume (V_1) to the nearest graduated units, repeat the tapping an additional 750 times and measure the tapped volume (V_2) to the

nearest graduated units. If the difference between the two volume is less than 2 % then final the volume (V_2). Calculate the tapped bulk density in gm/ml by the following formula:

Tapped density = Weight of powder / Tapped volume

Compressibility Index[96]

It is one of the most important parameter to characteristic the nature of powders and granules. The Compressibility Index of the powder blend was determined by Carr's compressibility index. It is a simple test to evaluate the BD and TD of a powder and the rate at which it packed down. It can be calculated from the following formula:

Carr's Index (%) = [(TD – BD) X 100] / TD

Hausner's Ratio:

The Hausner's ratio is a number that is correlated to the flowability of a powder or granular material.

Hausner's Ratio = TD / BD

Table 6: Effect of Carr's Index and Hausner's Ratio on Flow Property

Compressibility Index (%)	Flow Character	Hausner Ratio
≤ 10	Excellent	1.00–1.11
11–15	Good	1.12–1.18
16–20	Fair	1.19–1.25
21–25	Passable	1.26–1.34
26–31	Poor	1.35–1.45
32–37	Very poor	1.46–1.59
>38	Very very poor	>1.60

Angle of repose

The angle of repose of API powder was determined by the funnel method. The accurately weight powder blend were taken in the funnel. The height of the funnel was adjusted in such a way the tip of the funnel just touched the apex of the powder blend. The powder blend was allowed to flow through the funnel freely on to the surface. The diameter of the powder cone was measured and angle of repose was calculated using the following equation.

$$\tan \theta = h/r$$

Where, h and r are the height and radius of the powder cone respectively.

Table 7: Ingredients and Their Function

Sr. No.	Ingredients	Function	Normal Range (%)
1.	Telmisartan	API	16-24
2.	Sorbitol	Diluent	40-70
3.	Povidone	Binder	6-8
4.	Meglumine	Basic agent	10-12
5.	Sodium Hydroxide	Basic agent	2
6.	Sodium Starch Glycolate	Disintegrant	4-7
7.	Magnesium Stearate	Lubricant	1-2

Analytical Method Development [93]

- Calibration Curve of Telmisartan

Calibration curve of Telmisartan was taken in pH 7.5 phosphate buffer.

- Preparation of Reagents

(i) pH 7.5 phosphate buffer:

Prepared by dissolving 13.61 gm of Potassium dihydrogen phosphate in about 800 ml of water, adjusting with 2 M Sodium hydroxide to a pH of 7.5, and diluting with water to 1000 ml.

(ii) Standard (Stock) solution:

An accurately weighed 100 mg of Telmisartan (Drug) was dissolved and diluted to 1000 ml with pH 7.5 Phosphate buffer to produce 100µg/ml.

(iii) Sample solution:

Different dilution of stock solution with pH 7.5 Phosphate buffer were made to obtain solution having concentration 50, 60, 70, 80, 90, 100, 110, 120, 130, 150 µg/ml. Absorbance of each solution was measured at 296 nm using Shimadzu UV/Visible double beam spectrophotometer by using pH 7.5 Phosphate buffer as a reference standard. The standard curve was generated for the entire range from 50 to 150 µg/ ml.

Calibration curve of Telmisartan (drug) in pH 7.5 Phosphate buffer has been shown below. The concentration and absorbance data has been shown in table. From calibration curve of the drug it has been seen that the relation between concentration and absorbance was linear (R^2=0.9993).

Table 8: Absorbance at Different Concentration of Telmisartan

Sr. No.	Concentration (µg/ ml)	Absorbance			Avg. Absorbance Mean ± SD (n= 3)
		A1	A2	A3	
1	50	0.472	0.482	0.464	0.473±0.009
2	60	0.59	0.596	0.584	0.590±0.006
3	70	0.696	0.69	0.689	0.692±0.004
4	80	0.804	0.798	0.794	0.799±0.005
5	90	0.887	0.897	0.877	0.887±0.010
6	100	0.999	0.989	0.984	0.991±0.008
7	110	1.093	1.085	1.081	1.086±0.006
8	120	1.189	1.175	1.174	1.179±0.008
9	130	1.289	1.285	1.274	1.283±0.008
10	150	1.492	1.501	1.485	1.493±0.008
Equation y = 0.01x-0.015					
R-Square Value = 0.9993					

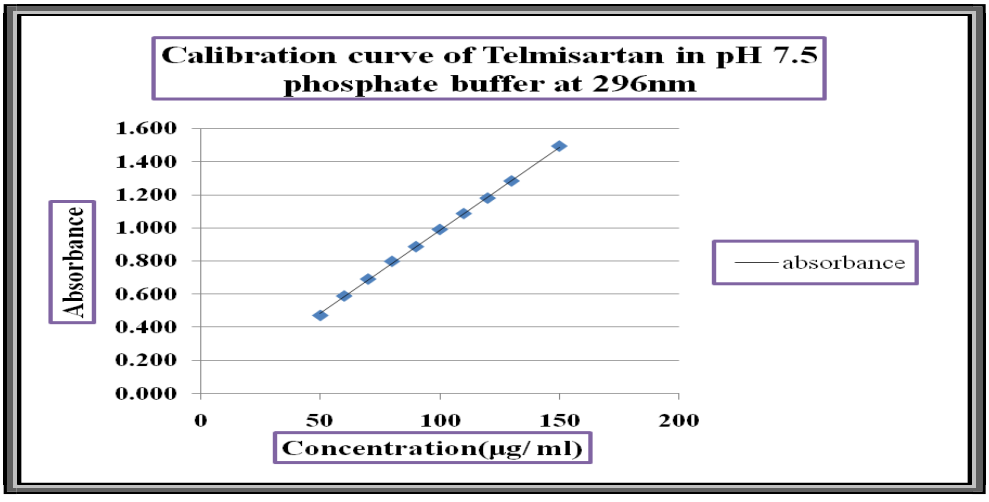


Figure 1: Calibration Curve of Telmisartan in pH 7.5 Phosphate Buffer at296nm

Physical Parameters and In-vitro Release Study of Innovator Product

Dissolution Parameter:

Medium: pH 7.5 Phosphate buffer
Volume: 900ml
Apparatus: USP-II (Paddle)
RPM: 75 rpm
Time point: 10, 15, 20, 30, 45 & 60 (min)
Temperature: 37 ± 0.5°C

Formulation and Optimization

Table 9: Formula of Trial Batches F1 to F4

Trial Ingredients	F1	F2	F3	F4
Telmisartan	80	80	80	80
Mannitol	164	163	174.5	162
Povidone (PVP K 25)	24	24	24	24
Sodium Carbonate	50	50	50	50
Sodium Hydroxide	-	1	2	2
Sodium starch glycolate	25	25	12.5	25
Magnesium Stearate	7	7	7	7
Purified water	q.s.	q.s.	q.s.	q.s.
Tablet Weight	**350 mg**	**350 mg**	**350 mg**	**350 mg**

Table 10: Formula of Trial Batches F5 to F10

Trial Ingredients	F5	F6	F7	F8	F9	F10
Telmisartan	80	80	80	80	80	80
Sorbitol	219.78	207.28	184.78	179.78	174.78	167.28
Povidone (PVP K 25)	24	24	24	24	24	24
Sodium Carbonate	-	-	-	-	-	-
Sodium Hydroxide	6.72	6.72	6.72	6.72	6.72	6.72
Meglumine	-	-	35	40	45	40
Sodium starch glycolate	12.5	25	12.5	12.5	12.5	25
Magnesium Stearate	7	7	7	7	7	7
Purified water	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.
Tablet Weight	**350 mg**	**350mg**	**350mg**	**350mg**	**350mg**	**350 mg**

Method of Preparation of Telmisartan IR Tablet

Granulation liquid or spray-solution:

Measured quantity of purified water was taken into a suitable stainless-steel vessel at atemperature of between 20-40°C. In sequence, measured quantity of Sodium carbonate, Sodium hydroxide was dissolved in the purified water and Telmisartan was dissolved in the above solution under intensive stirring until a virtually clear solution was obtained.

Granulation:

Measured quantity of Mannitol and Povidone (PVP K 25) were shifted through 40# sieve and mixed in the RMG and sprayed with granulation liquid. Granules were placed into a fluid bed dryer for drying followed by screening step.

Process data granulation:

Inlet air temperature: 80-100°C

Spraying rate: 500-900 ml/min

Process data drying step:
Inlet air temperature: 80 -100°C
End of drying: Gut temperature more than 70°C
Duration of drying: about 5 minutes
Process data screening step:
The granules were screened by using comil screen machine with a mesh size of 1.5 mm.

Final mixture for preparation of tablet formulation:
Measured quantity of Sodium starch glycolate and Magnesium stearate were shifted through 20# sieve and mixed with screened granules using a conta blender with a revolution of 10 rpm for about 15 min thus producing the final mixture.
Tablet compression:
Final blend was compressed using a suitable rotary tablet press and 16 station tabletcompression machine.
Process parameters for tabletting:
Tablet punch size: 12/32 SC PL/PL
Compression force: 7 (5-10) KN
The tablet hardness can be adjusted by variation of the main compression force.

Result & Discussion
From the above DSC Study and physical observation it was concluded that there was no significant Drug-Excipients interaction was observed as the DSC trace of API showed asharp endothermic peak at 159°C. In the DSC trace of the mixture of API and excipients, the sharp endothermic peak observed neared to 159°C, in the majority of case. Melting endotherm of the drug was well preserved with a slight change in terms of broadening of peak or shifting towards the lower temperature. Thus these minor changes in the melting endotherm of drug could be due to the mixing of drug and excipients, which lowers thepurity of each component in the mixture and may not necessarily indicating potential incompatibility.
Above study states that there was not any type of color change or lumps were formed.
Evaluation of Powder Blend
The powder blends of trial batches were evaluated for angle of repose, LBD, TBD,compressibility index.

Table 11: Result of Evaluation of Powder Blend of Trial Batches F1 to F4

Powder blend	Angle of Repose	Loose Bulk Density	Tapped Bulk Density	Carr's Index	Hausner's Ratio
F1	21.89	0.56	0.67	16.41	1.19
F2	25.46	0.59	0.71	16.9	1.20
F3	23.78	0.53	0.69	23.18	1.30
F4	25.14	0.61	0.74	17.56	1.21

Table 12: Result of Evaluation of Powder Blend of Trial Batches F5 to F10

Powder blend	Angle of Repose (^{0})	Loose Bulk Density (g/ml)	Tapped Bulk Density (g/ml)	Carr's Index (%)	Hausner's Ratio
F5	25.31	0.56	0.72	22.22	1.28
F6	22.28	0.58	0.76	26.31	1.31
F7	21.46	0.57	0.70	18.57	1.11
F8	22.91	0.62	0.71	12.68	1.15

F9	24.39	0.63	0.72	12.50	1.14
F10	23.21	0.61	0.73	16.44	1.19

The results of angle of repose and compressibility index ranged from 21.89 to 26.16 and 16.41 to 23.18 respectively. The results of Hausner's ratio ranged from1.19 to 1.30. The results of angle of repose (<30) indicate good flow properties of the powder based on table 6.1. This was further supported by lower compressibility index values. Generally, compressibility index values up to 25% results in Fair to passable flow properties.

Evaluation of Tablets

The formulations were evaluated for different parameters shown in the table below:

Table 13: Result of Evaluation of Tablets of Trial Batches F1 to F4

Parameters	**Trial batches**			
	F1	**F2**	**F3**	**F4**
Hardness (kP)	6-8	6-8	7-8	6-8
Thickness (mm)	2.84	2.81	2.89	2.85
Friability (%)	0.21	0.17	0.29	0.14
Avg. Wt. (mg)	353	357	349	352
Disintegration time(min)	12-13	11-12	12-13	10-11

In-Vitro Dissolution study

In-vitro dissolution study of trial batches F1 to F4 were carried out. Result of release study wasshown in the table 14 and comparative dissolution profile was shown in fig. 2.

Table 14: Result of In-vitro Release of Trial Batches F1 to F4

pH 7.5 Phosphate buffer, 900ml, USP - II (Paddle) Apparatus, 75 rpm				
Time (min)	**Trial batches**			
	F1	**F2**	**F3**	**F4**
0	0	0	0	0
10	21	17	18	22
15	28	24	23	29
20	34	32	29	33
30	40	40	36	48
45	45	48	51	60
60	47	51	62	65

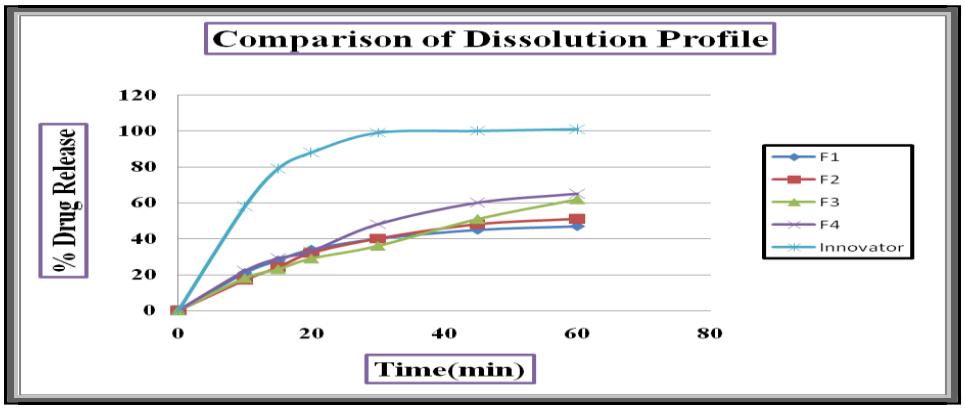


Figure 2: Comparative Dissolution Profile of Trials F1 to F4 and Innovator

The results of in-vitro dissolution study of trial batches F1 to F4 were carried out. Results were shown that drug was not release properly in the specific time compared to the targeted drug release.

In further formulation development process, trial batches F5 and F6 were develpoed by incorporation of Sodium hydroxide for dissolve the drug as it was soluble in basic media and Sodium hydroxide was strong base in compare to Sodium carbonate. Drug release profile of trails F5 and F6 were comparatively better than above batches but not achieve the desired targeted release. Sodium hydroxide was strong base and its maximum limit was upto 2% so we can not add more than that as it is toxic. So in the further trials Sodium hydroxide was used in combination with other basic agent to improve the dissolution profile. In the futher batches (F7 to F10) Meglumine was used in combination with Sodium hydroxide by changing the ratio of Meglumine and SSG. In these batches combition of Sodium hydroxide and Meglumine help to dissolve the drug and SSG also help to achieve the desired drug release profile.

Result of powder blend and and all parameters of tablets are within the limit. The result with combination of Meglumine and Sodium hydroxide show better release compared to Sodium hydroxide alone and combination of Sodium carbonate and Sodium hydroxide. Batch F5 and F6 show more drug release compare to F1 to F4 but not desired. Where as in case of combition of Sodium hydroxide and Meglumine (F7 to F10) show desired release profile compared to above batches from that optimize batch was selected on the basis of Similarity Factor (f2).

Result of f2 values shows that batch F8 shows higher similarity factor (f2 values) compared to other batches. F8 shows an f2 value 88.53 which is greater than 50 as shown in table 5.21. Based on similarity factor and dissolution, F8 is considered as optimized formula.

In-vitro drug release study show that after 1, 2 and 3 month f2 value obtained was 84.29,

79.27 and 86.79 respectively. This shows that drug release profile obtained was match with drug release profile of marketed reference product. Assay results were within the acceptance criteria. The related substance results showed that individual maximum impurity below 0.1% and total maximum impurity below 1.0%.

Stability result shows that there was no change in the formulation after 3 month accelerated stability study. It indicates that prepared formulation of Telmisartan was stable.

Summary & Conclusion

Formulation development work has been preceded with preformulation studies including analytical investigations, choice of the analytical methods, standardization and validation of the procedure and preliminary formulation trials. There is a need for selection of suitable excipients, which are compatible with drugs and among themselves and also physiologically safe and biocompatible. Preliminary idea about the behavior of the dosage form formulated, using the selected ingredients and their singular and collective effect and physicochemical and pharmaceutical properties of the dosage form also needs to be studied during this phase. In the present work efforts have been made to develop immediate release tablet of Telmisartan using excipients which shows dissolution profiles as per USP monograph.

In present work various preformulation parameters such as organolaptic properties, flow properties and particle size distribution of API have been studied from such results it was found that API has fair flow properties. The Drug-Excipients compatibility study was carried out by Differential Scanning Calorimetry at 40°C/ 75% RH condition for 1 month. From the above DSC Study and physical observation it was concluded that there was no significant Drug-Excipients interaction was observed as the DSC trace of API showed a sharp endothermic peak at 159°C. In the DSC trace of the mixture of API and excipients, the sharp endothermic peak observed neared to 159°C, in the majority of case. Thus these minor changes in the melting endotherm of drug could be due to the mixing of drug and excipients, which lowers the purity of each component in the mixture and may not necessarily indicating potential incompatibility.

In this case drug has poor water solubility and dissolves in strong base. So in batch F1 sodium carbonate was used to dissolve drug and SSG was used as disintegrant but desired release profile was not achieved. So in the further batches F2 to F4 mixture of sodium carbonate and sodium hydroxide used to properly dissolve the drug by changing the amount of SSG. But still the desired release profile was not achieved. Here basic agent was used in the

maximum limit so we cannot add more than the limit so we have to try with other basic agent or combination of thereof. In the batches F5 and F6 Sodium hydroxide alone used as basic agent which shows the better result compare to the above batches but not desired. So in batches F7 to F10 combination of sodium hydroxide and meglumine was used along with SSG, which shows desired release profile from that optimize batch was selected on the basis of Similarity Factor (f2).

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