World Journal of Pharmaceutical and Life Sciences
WJPLS
www.wjpls.org
SJIF Impact Factor: 6.129

FORMULATION AND EVALUTION OF TELMISARTAN FAST DISSOLVING TABLET BY DIRECT COMPRESSION METHOD

Bagwan Wasim*, Bagwan Jasmin, Khan Juber, Shaikh Shehzad, Shaikh Aaqueeb and Dr. G. J. Khan

Department of Pharmaceutics, Ali Allana College of Pharmacy, Akkalkuwa, Nandurbar-425415, MH India.

Corresponding Author: Bagwan Wasim
Department of Pharmaceutics, Ali Allana College of Pharmacy, Akkalkuwa, Nandurbar-425415, MH India.

Article Received on 22/06/2022 **Article Revised on 12/07/2022** **Article Accepted on 01/08/2022**

ABSTRACT

Telmisartan is an ACE inhibitor anti-hypertensive drugs which is insoluble in water, hence the drug may be slowly or incompletely dissolves in the gastro-intestinal tract. So, the rate of dissolution and therefore its bioavailability is less (bioavailability 42%). In the present study an attempt has been made to prepare Fast Dissolving tablets of Telmisartan by using Super disintegrants to increase the rate of drug release from dosage form to increase the dissolution rate and hence its bioavailability. The tablets were prepared by Direct Compression methods and the prepared blend and tablets were evaluated for their physicochemical properties and In-vitro dissolution study. The Disintegration time of Fast Dissolving tablets were increased by the addition of concentration of super disintegrants.

KEYWORDS: Telmisartan, Fast dissolving Tablets, Super disintegrants.

INTRODUCTION

Oral drug administration has been one of the most suitable and widely accepted by the patients for the delivery of most therapeutically active drugs. Various dosage forms like tablets, capsules and liquid preparations have been administered by oral route. But, due to some unsuitable physiological conditions of the gastrointestinal tract like relatively poor absorption, presence of various digestive enzymes of the gastrointestinal lumen and epithelium, first pass metabolism by hepatic enzymes, the administration of some drugs is affected. Also, it limits many drugs to reach into the therapeutic level. Hence to prepare Fast Dissolving tablets of Telmisartan to minimize the problems associated with drugabsorption through gastro-intestinal membrane, researchers have been developing intraoral drug delivery systems that will enhance the therapeutic drug level, avoids first-pass and gut-wall metabolism, increases the bioavailability of active medicament or improve convenience of dosing.

Telmisartan is a nonpeptide Angiotensin Receptor II (Type- ATI) Antagonist, That Cause Inhibition Of the action of Angiotensin II on Vascular Smooth Muscle in the Symptomatic Treatment of Hypertension. The Bioavailability of Telmisartan is Poor About 45%, which due to Extensive First Pass hepatic metabolism; The Bioavailability can be increase by Fast Dissolving Formulation. Conventional Telmisartan tablets available in market are not suitable where quick onset of action is required. To provide the patients with the most conventional mode of administration, there was a need to develop rapidly disintegrating dosage form, particularly one that Disintegrates and dissolves/disperses in saliva and can be administered without need of water.

MATERIAL AND METHODS

Telmisartan was used as active pharmaceutical ingredient which is angiotensin receptor II antagonist. Microcrystalline cellulose, Croscarmellose sodium and Sodium starch glycolate was used as super disintegrants. Mannitol was used as diluent, Sodium Lauryl Sulphate as solubility enhancer and Magnesium Stearate as lubricant.

PRE-FORMULATION STUDIES

Pre-formulation testing is an investigation of physical and chemical properties of a drug substance alone and when combined with excipients. It is the first development in the rationale development of the dosage forms. Pre-formulation studies yields necessary knowledge to develop suitable formulation for toxicological use. It gives information needed to define the nature of the drug substance and provide a dosage form. Hence, the following pre-formulation studies were performed for the obtained sample of drug.

Bulk Density

Bulk density of a compound various substantially with the method of crystallization, milling or formulation. Bulk density is determined by pouring pre-sieved

granules into a graduated cylinder via a large funnel and measure the volume and weight.
Bulk density = weight of granules Bulk volume of granules
Bulk density was expressed in g/cc.

Tapped Density
Tapped density is determined by placing a graduated cylinder containing a known mass of granules and mechanical tapper apparatus, which is operated for a fixed number of taps until the powder bed volume has reached a minimum volume. using the weight of the drug in the cylinder and this minimum volume, the taped density may be computed.
Tapped density = weight of granules Tapped volume of granules

Carr's Index (CI)
Carr's index is measured using the values of bulk density and tapped density. The following equation is used to find the Carr's index.
CI = (TD-BD) x100 TD

Where,
TD = Tapped density
BD = Bulk density

Hausner's Ratio
It indicates the flow properties of the powder and ratio of Tapped density to the Bulk density of the powder or granules.
Hausner's Ratio = Tapped density/Bulk density

Angle of Repose
The manner in which stresses are transmitted through a bead and the beads response to applied stress are reflected in the various angles of friction and response. The method used to find the angle of repose is to pour the powder ion a conical heat on a level, flat surface and measure the included angle with the horizontal.
$\tan\theta = h/r$

Where,
h= height of the heap
r= Radius of the heap

Preparation of Fast Dissolving Tablets of Telmisartan
The drug, Telmisartan equivalent to 20 mg and mannitol were mixed thoroughly in glass mortar using a pestle. super disintegrants (Microcrystalline cellulose, Croscarmellose sodium and Sodium starch glycolate) were incorporated in the powder mixture and finally magnesium stearate was added as lubricant and SLS was added as solubility enhancer. The whole mixture is then passed through sieve no.60 twice. Tablets were prepared using 8 mm round flat-faced punch of the rotary tablet machine compression force was kept constant for all formulation.

Table No. 1: Composition of Fast Dissolving Tablet of Telmisartan.

Sr No.	Ingredients (mg/ml)	F1	F2
1	Telmisartan	20	20
2	Microcrystalline cellulose	150	140
3	Crosspovidone	05	-
4	Croscarmellose Sodium	-	05
5	Sodium Starch Glycolate	-	05
6	Sodium Lauryl sulphate	05	08
7	Sodium Saccharin	15	15
8	Talc	05	02
9	Magnesium Stearate	-	03
	Tablet Weight	200	200

EVALUATION OF TABLETS
To design tablets and later monitor tablet production quality, quantitative evaluation and assessment of tablet chemical, physical and bioavailability properties must be made. The important parameters in the evaluation of tablets can be divided into physical and chemical parameters.

Physical Appearance
The general appearance of tablets, its visual identity and overall elegance is essential for consumer acceptance. The control of general appearance of tablet involves measurement of number of attributes such as tablet size, shape, colour, presence or absence of odour, taste, surface texture and consistency of any identification marks.

Hardness Test
This is the force required to break a tablet in a diametric compression. Hardness of the tablet is determined by Stock's Monsanto hardness tester which consists of a barrel with a compressible spring. The pointer moves along the gauze in the barrel fracture. The tablet hardness of 7Kp is considered as suitable for handing the tablet.

Tablet size and Thickness
Control of physical dimensions of the tablets such as size and thickness is essential for consumer acceptance and

tablet-tablet uniformity. The diameter size and punch size of tablets depends on the die and punches selected for making the tablets. The thickness of tablet is measured by Vernier Callipers scale. The thickness of the tablet related to the tablet hardness and can be used an initial control parameter. Tablet thickness should be controlled within a ±5%. In addition, thickness must be controlled to facilitate packaging.

Friability

This test is performed to evaluate the ability of tablets to withstand abrasion in packing, handling and transporting. Initial weight of 20 tablets is taken and these are placed in the Roche friabilator, rotating at 25rpm for 4min. The difference in the weight is noted and expressed as percentage. It should be preferably between 0.5 to 1.0%.

Weight variation of Tablets

It is desirable that all the tablets of a particular batch should be uniform in weight. If any weight variation is there, that should fall within the prescribed limits. Twenty tablets were taken randomly and weighed accurately. The average weight was calculated by,

Average weight = weight of 20 tablets/20

Disintegration Test

Disintegration time is considered to be one of the important criteria in selection the best formulation. To achieve correlation between disintegration time in-vitro and in-vivo, several methods were proposed, developed and followed at their convenience. One tablet was placed into each tube and the assembly was suspended into the 1000ml beaker containing water maintained at 37±20oc and operated the apparatus for 15 minutes. The assembly was removed from the liquid and the tablets were observed. If one or two tablets fail to disintegrate completely, repeat the test on 12 additional tablets. The requirement is met if not less than 16 of the total of 18 tablets tested are disintegrated.

Wetting Time

A piece of tissue paper folded twice was kept in a petri dish containing 6 ml of purified water. The tablet was placed on the tissue paper and allowed to wet completely. The time required for complete wetting of the tablet was then recorded.

In-Vitro Dissolution Study

The release rate of telmisartan from fast dissolving tablets was determined using United State Pharmacopoeia (USP) dissolution testing apparatus II (paddle method). The dissolution test was performed using 900 ml of 0.1N HCL pH 6.8 dissolution medium, at 37±0.5°C and 75 rpm. Sample volume of 10 ml was withdrawn at regular time intervals from a zone midway between the surface of dissolution medium and the top of rotating paddle not less than 1 cm apart from the vessel wall. The volume withdrawn was replaced by fresh volume of dissolution medium to maintain constant volume of medium. The filtered samples were analyzed spectrophotometrically at 291 nm using 0.1N HCl as a blank. Drug content in dissolution sample was determined by calibration curve.

RESULTS AND DISCUSSION

Pre-Compression Parameters

Powder ready for compression containing drug and various excipients were subjected for pre-compression parameters (Micromeritic properties) to study the flow properties of granules, to achieve uniformity of tablet weight.

Angle of Repose

The data obtained from angle of repose for all the formulations were found to be in the range of 29.900 and 34.40`. All the formulations prepared by both the methods showed the angle of repose less than 35, which reveals good flow property.

Bulk Density

Loose bulk density (LBD) and tapped bulk density (TBD) for the blend was performed. The loose bulk density and tapped bulk density for the entire formulation blend varied from 0.33 gm/cm3 to 0.39 gm/cm3 (direct compression method) and 0.33gm/cm3 to 0.38gm/cm3 (sublimation method) respectively.

Hausner's Ratio

Hausner's ratio of entire formulation showed between 1.19 to 1.34 indicates better flow properties.

Carr's Consolidation Index

The results of Carr's consolidation index or compressibility index (%) for the entire formulation blend ranged from 17.6% to 19.6%. The directly compressible granulations had shown excellent compressibility index values up to 15% result in good to excellent flow properties.

Table No. 2: Results Precompression Parameters.

Parameters	F1	F2
Angle of repose	32.3±0.04	32.6±0.02
Bulk density	0.32±0.04	0.36±0.12
Tapped density	0.42±0.08	0.47±0.07
Compressibility index	17.7±0.08	18.6±0.02
Hausner's ratio	1.21±0.02	1.19±0.12

Based on compressibility index and particle size distribution data, it was concluded that the blend showed good flow characteristics. Thus, the blend was compressed further to check the compression parameter.

Post-Compression Parameters

Hardness

The hardness of all the tablets prepared by both methods was maintained within the 3.00 kp to 5.00 kp. The mean hardness test results are tabulated in table no. 24 and 25.

Friability Test

The friability was found in all designed formulations in the range 0.01 to 0.05% to be well within the approved range (0.1 To 0.05% to be well within the approved range (less than 1%) The friability study results were tabulated in table

Weight Variation Test

The weight variation was found in all designed formulations in the range 200 to 205 mg. The mean weight variation test results. All the tablets passed weight variation test as the average percentage weight variation was within 7.5% i.e., in the pharmacopoeia limits.

Thickness

The mean thickness was (n=3) almost uniform in all the formulations and values ranged from 4.20±0.064 mm to 4.85 ± 0.016 mm. The standard deviation values indicated that all the formulations were within the range.

Wetting Time

A piece of tissue paper folded twice was kept in a petri dish containing 1 ml of purified water. The tablet was placed on the tissue paper and allowed to wet completely. The time required for complete wetting of the tablet was then recorded. The wetting time was found in the range of 20-40.

In Vitro Dispersion Time

The in vitro dispersion time is measured by the time taken to undergo uniform dispersion. Rapid dispersion within several minutes was observed in all the formulations. The in vitro dispersion time of Telmisartan prepared by direct compression and sublimation method were found to be in the range of 36 to 115 sec fulfilling the official requirements.

In Vitro Disintegration Time

Disintegrating study showed that the disintegrating times of the tablets decreased with increase in the concentration of cross-carmellose sodium, Crosspovidone. However, disintegration times increased with increase in the concentration sodium starch glycolate in the tablets. It indicates that increase in the concentration sodium starch glycolate had a negative effect on the disintegration of the tablets. The results are in consistent with other results. The disintegration times of Crosspovidone containing tablets are comparatively lower than tablets containing cross-carmellose sodium and sodium starch glycolate due to its rapid capillary activity and pronounced hydration with little tendency to gel formation with Crosspovidone. Thus, these results suggest that the disintegration times can be decreased by using wicking type disintegrants (Crosspovidone).

Drug Content

The drug content uniformity was performed for all the formulations and results are tabulated in table Three trials from each batch were analyzed spectrophotometrically. The average value and standard deviations of all the formulations were calculated. The percentage drugs content of the tablets was found to be between 99.20 of Telmisartan. The results were within the range and that indicated uniformity of mixing.

Table No. 3: Results of Evaluation Parameters.

Parameters	F1	F2
Average Hardness (Kp)	3.2 ± 0.25	3.1 ± 0.32
Thickness (mm)	4.2-4.4	4.1-4.4
Percentage of weight loss (%)	0.05±0.01	0.04±0.11
Average Weight (mg)	201.1	198.2
In-vitro dispersion time(sec)	40	38
Disintegration time(sec)	45	41
Wetting time(sec)	35	27
% Drug Content	98.70	99.20

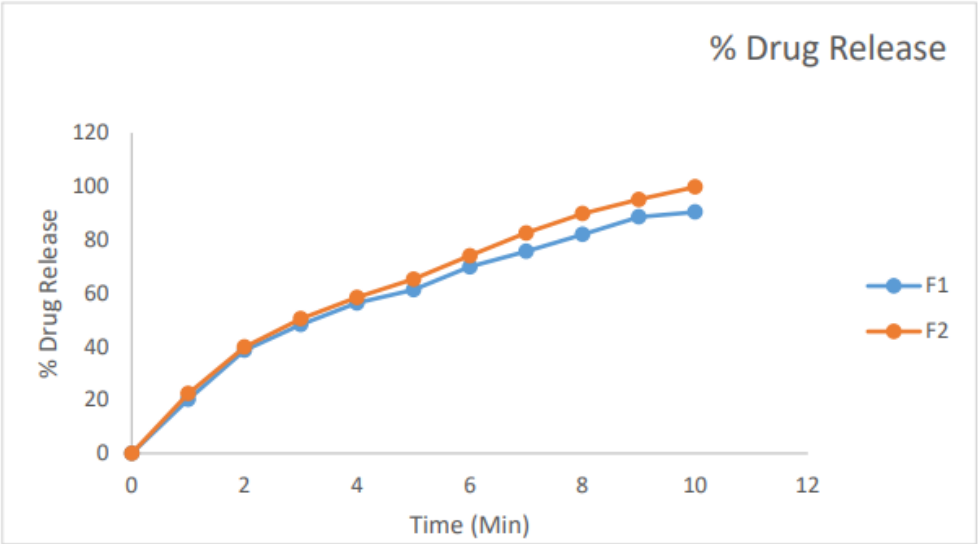

Fig No. 1 In-Vitro Release Profile of Formulations.

CONCLUSION

In accordance with present study, it was concluded that, the present investigated Telmisartan fast dissolving tablets can be an alternative dosage form for Telmisartan tablets and the rate of drug release increased from dosage form due to which there is increase in the dissolution rate. In addition, there is increase in the bioavailability of Telmisartan. Method of preparation is simple, cost effective and scalable.

ACKNOWLEDGEMENT

We are thankful to my respected guide and management Ali-Allana College of Pharmacy, Akkalkuwa for their support.

REFERENCES

1. Herbert A, Lieberman, Leon Lachman and Joseph B. Schwartz, Pharmaceutical Dosage Forms Tablets, 2003, 3rd edition, 201- 238.
2. Jantratid E., "Reported the bio wavier Monographs for immediately release solid dosage forms cimetidine", Journal of pharmaceutical Research, 2006; 17: 381.
3. Jacob Christensen and Vibeke Wallert Hamsen, Wet granulation in rotary processer and fluid bed: Comparison of granule and tablet properties, AAPS Pharma Sci Tech., Article 22, 2006, 7th edition.
4. Aulton M, Pharmaceutics, The Science Of Dosage Form Design, International student edition, published by Churchill Livingstone, 2002; 304-321.
5. Mahajan, HS., Rapidly disintegrating tablets for elderly patients. The pharma Review, 8th edition, 2005; 49-52.
6. Ansel H, Allen L and Jr. Popovich N, Ansel's Pharmaceutical Dosage Forms and Drug Delivery Systems, 8th edition, published by Lippincott Williams and Wilkins, 2004; 227-259.
7. Chen, GL., Kuo MK., 52nd edition, "Formulation Design for Pioglitazone Rapid Release Tablet", Chinese pharmaceutical Journal, 2000; 295-300.
8. Debjit Bhowmik, B.Jayakar, K.Sampath Kumar (2009). Design And Characterisation of Fast Dissolving Tablet of Telmisartan. International Journal of Pharma Recent Research: 1(1): 31-40.
9. Shailendra Kumar Singh, Dinanath Mishra, Rishab Jassal, Pankaj Soni (2009). Fast Disintegrating Combination Tablets of Omeprazole and Domiperidone. Asian Journal of Pharmaceutical and Clinical Research: 2(4).
10. Pooja Mathur, Kamal Saroha, Surender Verma, Navneet Syan and Ajay Kumar (2010). Mouth dissolving tablets: An overview on future compaction in oral formulation technologies. Pelagia Research Library, 1(1): 179-187.
11. Ghosh TK, Pfister WR. Intraoral delivery systems: an overview. In: Ghosh TK, Pfister WR. Drug delivery to the oral cavity. New York: CRC Press, Taylor and Francis group, 2005; 1-40.
12. R.Yarwood, ―Zydis — A Novel, Fast Dissolving Dosage Form,‖Man. Chem., February 1990; 36–37.
13. Brahmeshwar Mishra * Dali Shukla, Subhashis Chakraborty, Sanjay Singh (2009). Mouth Dissolving Tablets I: An Overview of Formulation Technology. Sci Pharm., 2009; 76: 309–326.
14. Modasiya M.K., Lala I.I., Prajapati B.G., Patel V.M. and Shah D.A. (2009). Design and Characterization of Fast Disintegrating Tablets of Piroxicam. International Journal of PharmTech Research, 1(2): 353 -357.