Research Article

Formulation and Evaluation of Fast Dissolving Tablet of Telmisartan

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ABSTRACT

The purpose of this research was to prepare Fast dissolving tablet of Telmisartan. The concentration of Crosscaramelose sodium, Sodium starch glycolate and crosspovidone was varied to formulate the tablet. The tablet was prepared by Direct compression method .The evaluation that were used are Thickness, Hardness. Weightvariation. Disintigeration time, Friability test, Invitro drug release. The result was found to be that among the six formulation the f6 formulation was found to be the best as it shows maximum release of 99.88%.

Keywords: Mouth dissolving tablet, Conventional techniques, Rapid Disintegration.

INTRODUCTION

A fast-dissolving drug delivery system, in most cases, is a tablet that dissolves or disintegrates in the oral cavity without the need of water or chewing. Most fast-dissolving delivery system films must include substances to mask the taste of the active ingredient. This masked active ingredient is then swallowed by the patient's saliva along with the soluble and insoluble excipients. These are also called melt-in-mouth tablets, repimelts, porous tablets, oro-dispersible, quick dissolving or rapid disintegrating tablets.

An ideal Properties of FDT

Require no water for oral administration, yet dissolve / disperse/ disintegrate in mouth in a matter of seconds.

Have a pleasing mouth feel. Have an acceptable taste masking property. Be harder and less friable Leave minimal or no residue in mouth after administration Exhibit low sensitivity to environmental conditions (temperature and humidity). Allow the manufacture of tablet using conventional processing and packaging equipments[5].

Advantages of MDT

a. No need of water to swallow the tablet[6].
b. Can be easily administered to pediatric, elderly and mentally disabled patients.
c. Accurate dosing[7] as compared to liquids.
d. Dissolution and absorption of drug is fast, offering rapid onset of action.
e. Bioavailability of drugs is increased[8]as some drugs are absorbed from mouth, pharynx and esophagus through saliva passing down into the stomach[9].
f. Advantageous over liquid medication in terms of administration as well as
g. Transportation
h. First pass metabolism is reduced, thus offering improved bioavailability and thus reduced dose and side effects.
i. Free of risk of suffocation due to physical obstruction when swallowed, thus
j. offering improved safety.
   i. Suitable for sustained/controlled release actives[10].
   ii. Allows high drug loading[3].

Disadvantage[11,12]

a. Fast dissolving tablet is hygroscopic in nature so must be keep in dry place.
b. Some time it possesses mouth feeling.
c. MDT requires special packaging for properly stabilization & safety of stable product.
d. The tablets usually have insufficient mechanical strength. Hence, careful handling is required
e. The tablets may leave unpleasant taste and/or grittiness in mouth if not formulated properly[2].

Telmisartan is an angiotensin II receptor antagonist (ARB) used in the management of hypertension. Generally, angiotensin II receptor blockers (ARBs) such as telmisartan

bind to the angiotensin II type 1 (AT1) receptors with high affinity, causing inhibition of the action of angiotensin II on vascular smooth muscle, ultimately leading to a reduction in arterial blood pressure. Recent studies suggest that telmisartan may also have PPAR-gamma agonistic properties that could potentially confer beneficial metabolic effects. Telmisartan is an orally active nonpeptide angiotensin II antagonist that acts on the AT_1 receptor subtype. It has the highest affinity for the AT_1 receptor among commercially available ARBS and has minimal affinity for the AT_2 receptor. New studies suggest that telmisartan may also have PPARγ agonistic properties that could potentially confer beneficial metabolic effects, as PPARγ is a nuclear receptor that regulates specific gene transcription, and whose target genes are involved in the regulation of glucose and lipid metabolism, as well as anti-inflammatory responses. This observation is currently being explored in clinical trials. Angiotensin II is formed from angiotensin I in a reaction catalyzed by angiotensin-converting enzyme (ACE, kininase II). Angiotensin II is the principal pressor agent of the renin-angiotensin system, with effects that include vasoconstriction, stimulation of synthesis and release of aldosterone, cardiac stimulation, and renal reabsorption of sodium. Telmisartan works by blocking the vasoconstrictor and aldosterone secretory effects of angiotensin II.
The aim of the present study was to formulate and evaluate fast dissolving tablet of telmisartan using different suprdisintigerant

MATERIAL AND METHODS

Telmisartan was received as a gift samples from Troica Pharmaceutical Lmtd,. Dehradun India. Magnesium stearate , Talc , Camphor , Manitol , Micro Crystaline Cellulose (MCC),, Sodium starch glycolate and ethyl cellulose (EC) were gift from CDH laboratory New Delhi and Crosss caramalose Shreya Pvt.Ltd. Roorkee respectively.

INVESTIGATION OF PHYSICOCHEMICAL COMPATIBILITY OF DRUG AND SUPER DISINTIGERANTS

The physicochemical compatibility between Telmisartan and superdisintigerant used in the preparation of fast dissolving tablet was studied by fourier transform infrared (FTIR-Perkin elmer, India) spectroscopy.
The infrared (IR) spectra were recorded using an FTIR by the KBr pellet method and Neuzol method. Spectra were recorded in the wavelength region between 4000 and 400 cm–1. The spectra obtained for Telmisartan, superdisintigerant, and physical mixtures of Telmisartan with superdisintigerant were compared.

Preformulation studies

Drug

Organoleptic characteristics

The colour, odour, and taste of the drug were characterized and recorded. The results are shown in Table 1.

Determination of Melting Point

Melting point of Telmisartan was determined by capillary method. Fine powder of Telmisartan was filled in capillary tube (previously sealed at one end). The capillary tube inserted in sample holder of melting point apparatus and a thermometer is also placed in the apparatus. The temperature at which powder melted was noticed (result shown in table 2).

Solubility

The solubility aspect of telmisartan and/or the salts of the invention is characterized in that telmisartan or its salt exhibit solubility above 50 µg/ml, preferably above 500 µg/ml, more preferably above 5 mg/ml or 100 mg/ml in phosphate buffer at pH 6.76, additionally having sodium taurocholate in concentration 2,5 mM and lecitin in concentration 0,5 mM after stirring 50 mg for 30 minutes at 37°C in 100 ml baker at 600 rpm.

Melting point

Small amount of drug was filled in the capillary tube which is being sealed from one side then placed in the instrument with a thermometer placed in it the melting point is determined by capillary method.

Table 1: Evaluation of organoleptic properties of powder

Excipients	Description	
	Appearance	Odour
Telmisartan	White powder	Odourless
Manitol	White crystalline powder	Odourless
Starch	White to light yellow powder	Odourless
Camphor	White crystals	Characterstic
Micro crystalline cellulose	White powder	Odourless
Sodium starch glycolate	White powder	Odourless
Cross carmelose sodium	White powder	Odourless
Magnesium stearate	Light white powder	Slight
Talc	Light to dark green, brown, white powder	Odourless

Calibration curve of Telmisartan

Preparation of Standard Calibration Curve of Telmisartan

A 20mg of standard Telmisartan was weighed and transferred to a 100ml volumetric flask and dissolved in 50ml of Diluent. The flask was sonicating for 15min. and volume was made up to the mark with Diluent. From this stock solution working standard solution was prepared by Further 5.0ml was transferred in 100ml volumetric flask and Diluent was added up to the mark to give a solution containing 10µg/ml Telmisartan. Appropriate volume of aliquots from standard Telmisartan stock solution was transferred to different volumetric flasks of 200ml capacity .The volume was adjusted to the mark with the Diluent to obtain the concentration of 4, 6, 8, 10, 12 and 14µg/ml. Calibration curve of each solution against the Diluent was recorded at 296nm was measured and the plot of absorbance v/s concentration was plotted. The straight-line equation was determined (Figure 4).

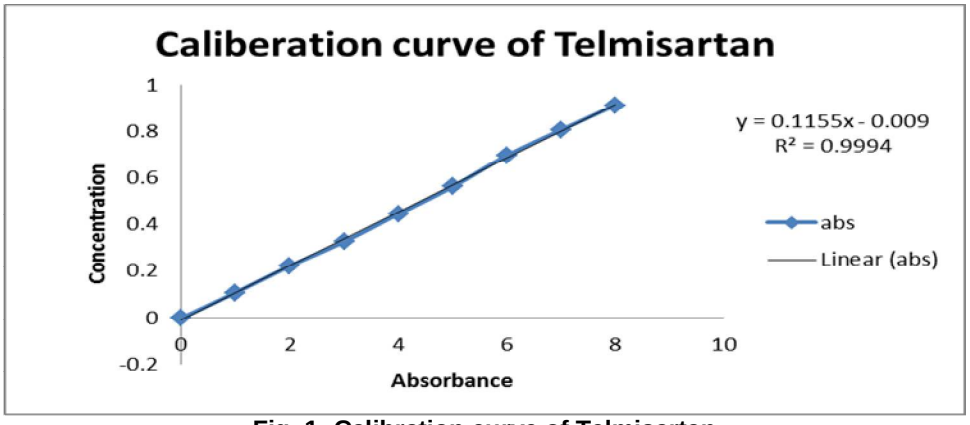

Fig. 1: Calibration curve of Telmisartan

Formulation chart

Table 2: Formulation chart

Ingredients	Formulation code					
	F1	F2	F3	F4	F5	F6
Telmisartan	10	10	10	10	10	10
Sodium starch glycolate	2.5	3.75				
Micro crystalline cellulose	50	50	50	50	50	50
Cross caramelose sodium	-	-	3	6	-	-
Sodium lauryal sulphate	1	1	1	1	-	-
Magnesium stearate	3	3	3	3	3	3
Talc	-	-	-	-	1	1
Camphor	-	-	-	-	30	35
Menthol	2	2	2	2	-	-
Aspartam	-	-	-	-	10	10
Mannitol total up to	100	100	100	100	100	100

METHODOLOGY

Direct compaction

Direct compression method is the easiest way to manufacture tablets. Conventional equipment, commonly available excipients and a limited number of processing steps are involved in direct compression.In this method drug with other excepient is mixed in motar pistel and the nixture thus obtained is compressed into tablets through tablet punching machine.

FTIR

In this powdered drug is taken and then dried for an hour in an oven .The kbr is also dried in an oven the drug and kbr is then mixed and palates are made through the insntrument by applying pressure now these palates are placed in the FTIR and the absorbance is being absorbed in the form of graphs.

Flow property of powder

The simplest way for measurement of free flow of powder is compressibility, a indication of the ease with which a material can be induced to flow is given by Compressibility Index. The value below 15% indicates a powder with give rice to good flow properties, whereas above 25% indicate poor flowability. Which is calculated follows. % C.I. = ρt - ρb ρt ˣ 100

Hausner ratio[26]

Hausner ratio is an indirect index of ease of powder flow. Hosner ratio is the ratio of tapped density to bulk density. Lower the value of Housner ratio better is the flow property. Powder with Housner ratio less than 1.18, 1.19, 1.25, 1.3- 1.5 and greater the 1.5 indicate excellent, good, passable, and very poor, respectively. It is calculated by following formula. Hausner ratio = ρt ρt

Porosity[25,28]

Percent relative porosity (ε) was obtained using the relationship between apparent density (ρapp) and true density (ρtrue) which is calculated by following formula. ε = (1 - ρapp / ρtrue) ˣ 100

Voide Volume[25]

Voide volume(V) was obtained by difference between bulk volume(Vb) and tapped volume (Vp).Voide volume can be calculated by following formula.

Angle of repose[26,28]

The angle of repose was determined using funnel method. Funnel that can be fit vertically with stand at 6.3 cm. height. The opening end of funnel are closed with thumb until drug are poured. The 5 gm of powder was poured into funnel that can be raised vertically until a maximum cone hight (h) was obtained. Radius of the heap (r) was measured and the angle of repose (Ɵ) was calculated using the formula.

Evaluation of Mouth dissolving Tablets

Thickness[29]

Tablet thickness can be measured using a simple procedure. 5 tablets were taken and their thickness was measured using Varnier calipers.

Hardness[27,30]

It is the force required to break a tablet by compression in the radial direction, it is an important parameter in formulation of mouth dissolve tablets because excessive crushing strength significantly reduces the disintegration time.In the present study the crushing strength of the tablet was measured us-ing Pfizer hardness testers. An average of three observations is reported.

Uniformity of weight[31,27]

I.P. procedure for uniformity of weight was followed, twenty tablets were taken and their weight was determined individually and collectively on a digital weighing balance. The average weight of one tablet was determined from the collective weight. The weight variation test would be a satisfactory method of determining the drug content uniformity.

Disintegration time[31]

The test was carried out on 6 tablets using the apparatus specified in I.P.-1996 distilled water at 37ºC ± 2ºC was used as a disintegration media and the time in second taken for complete disintegration of the tablet with no palatable mass remaining in the apparatus was measured in seconds

In-vitro drug release[31]

The development of dissolution methods for ODTs is comparable to the approach taken for conventional tablets, and is practically identical. Dissolution conditions for drugs listed in a pharmacopoeia monograph, is a good place to start with scouting runs for a bioequivalent ODT. Other media such as 0.1N HCl and buffers (pH - 4.5 and 6.8) should be evaluated for ODT much in the same way as their ordinary tablet counter parts. The USP 2 Paddle apparatus is used for this purpose which is the most suitable and common choice for orally-disintegrating tablets, with a paddle speed of 50 rpm commonly used. Typically the dissolution of ODT is very fast when using USP monograph conditions; hence slower

paddle speeds may be utilized to obtain a profile. The USP 1 Basket apparatus may have certain applications but sometimes tablet fragments or disintegrated tablet masses may become trapped on the inside top of the basket at the spindle where little or no effective stirring occurs, yielding irreproducible dissolution profiles.

Friability test[32,27]

Friability of the tablets was determined using Roche friability (Electrolab, Mumbai). This device subjects the tablets to the combined effect of abrasions and shock in a plastic chamber revolving at 25 rpm and dropping the tablets at a height of 6 inches in each revolution. Preweighed sample of tablets was placed in the friabilator and were subjected to 100 revolutions. Tablets were de dusted using a soft muslin cloth and reweighed. The friability (f) is given by the formula. f = (1- W0 / W) × 100 Where, W0 is weight of the tablets before the test and W is the weight of the tablet after the test.

COMPATABILITY OF DRUG AND POLYMER

The physicochemical compatibility between Telmisartan and polymers used in the preparation of fast dissolving drug delivery system was studied by fourier transform infrared (Perkin Elmer,India) spectroscopy.

The infrared (IR) spectra were recorded using an FTIR by the KBr pellet method. Spectra were recorded in the wavelength region between 4000 and 400 cm–1. The spectra obtained for Telmisartan, and physical mixtures of Telmisartan with suprdisintigerant were compared.

RESULT AND DISCUSSION

Organoleptic properties

The colour ,odour and taste of the drug and polymer are recorded in Table 1.

Solubility

The solubility of drug was checked with Water, DMSO , Ethanol . It is given in Table 2.

Calibration curve

It is shown in Figure 1.

Compatibility study of Drug and superdisintigerant

To check the compatibility between the selected polymers and drug used in the formulation IR Study was carried out. The main reason to carry out this study was to confirm that there should be complete physical entrapment of drug into the polymer matrix with no mutual interaction. IR spectra were taken for sample like pure drug and mixture of drug – polymer which are dried with mixing at room temperature (18-22). Comparision of shifting of major functional peaks was observed for the identification of incompatibility. No shifting of functional peaks with no overlapping of characteristic peaks, no appearance of new peaks were observed when the comparision of spectra was done. FTIR of drug and drug polymer mixture are given in Figure 4.

RESULTS AND DISCUSSION

Physiochemical characterization of tablets

The flow properties of powder mixture are important for the uniformity of mass of tablet the flow of powder mixture was before compression of tablets. The value of precompressional parameters were within prescribed limits as per USP XXVII and indicates good flow properties .The results are shown im table 3 .

The post compresssional parameters results are shown in table 4 in all formulations the hardness test indicates good mechanical strength.the hardness of all tablets was found between – to- .friability of all formulations was less than 1%, which shows the tablet has good mechanical resistance. Drug content was found to be high (≥100.86 %) and uniform in all formulations.the tablet thickness was found to be 3.12 to 3.30 mm. The weight variation results revealed that average percentage deviation of 20 tablets of each formulae was less than ±7.5%, which provide good uniformity in all formulations..The disintigeration time of all tablets found to be in the range of 17 to 44 sec. The tablets prepared by direct compression technique rapidly disintigerates the tablet it may be due to their lowest hardness which was responsible for faster disintigeration Wetting time is closely related to the inner structure of the tablets. The wetting time of all formulation were found to be in the range of- to- sec. the dissolution profiles of all formulations are shown in table. Out of six formulation, the formulation F4, shows faster drug release .in-vitro profile of telmisartan is shown in fig 2 and table 5.

Table 2: Evaluation of pre-formulation parameters of powder

Excipients	Solubility	Melting point
Telmisartan	Water (Practically insoluble) , Ethanol(slightly soluble) DMSO(1mg/mL)	261-263^{0}C

Table 3: Pre–compressional parameters of Telmisartan FDTs

Formulation code	Bulkdensity (gm/cm^3)	Tapped density (gm/cm^3)	Angle of Repose (0)	Compressibility Index (%)	Hausner ratio
F1	0.50±0.006	0.62±0.01	31.19±1.0	15.65±0.12	1.16±0.11
F2	0.52±0.008	0.64±0.03	28.65±1.20	14.06±0.18	1.19±0.08
F3	0.55±0.005	0.63±0.02	21.34±0.12	16.64±0.11	1.22±0.05
F4	0.51±0.007	0.63±0.04	23.19±0.09	19.63±0.16	1.20±0.09
F5	0.54±0.004	0.65±0.02	18.32±0.15	14.84±0.14	1.18±0.04
F6	0.50±0.003	0.66±0.05	20.25±0.11	15.62±0.16	1.17±0.06

Table 4: Post –compressional parameters of Telmisartan FDTs

Formulation code	Weight variation (mg)±SD	Thickness (mm))±SD	Hardness (kg/cm^2))±SD	Friability (%)
F1	97±3.21	3.21±0.20	2.6±0.29	0.60
F2	101±2.51	3.16±0.34	2.4±0.12	0.62
F3	98±3.12	3.25±0.12	2.5±0.14	0.54
F4	100±0.52	3.12±0.31	2.8±0.28	0.70
F5	99±1.08	3.30±0.14	2.7±0.15	0.65
F6	96±4.52	3.22±0.11	2.4±0.34	0.53

Table 5: Cumulative percentage drug release of Telmisartan

Time (min)	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0
5	40.60	43.30	50.35	56.78	41.78	42.36
10	65.45	72.68	79.48	81.32	63.78	67.88
15	70.38	76.25	83.20	84.12	68.88	69.58
20	78.72	80.85	85.85	87.66	73.58	75.28
25	82.56	84.29	97.98	98.84	80.75	80.65
30	89.88	95.58	98.85	99.88	87.38	88.98

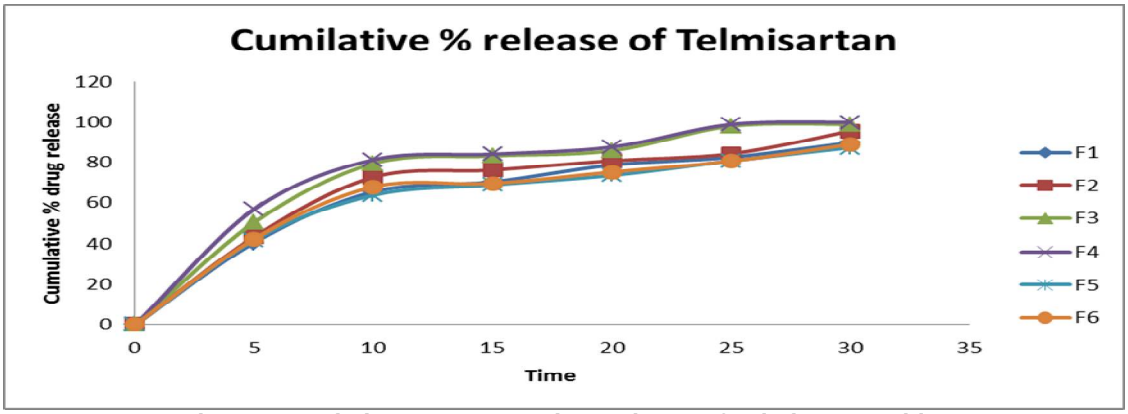

Fig. 2: Cumulative percentage drug release of Telmisartan tablet

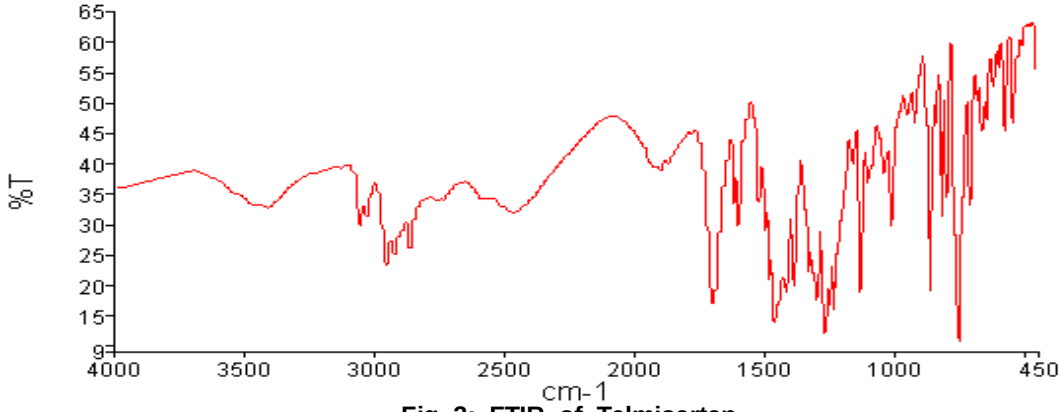

Fig. 3: FTIR of Telmisartan

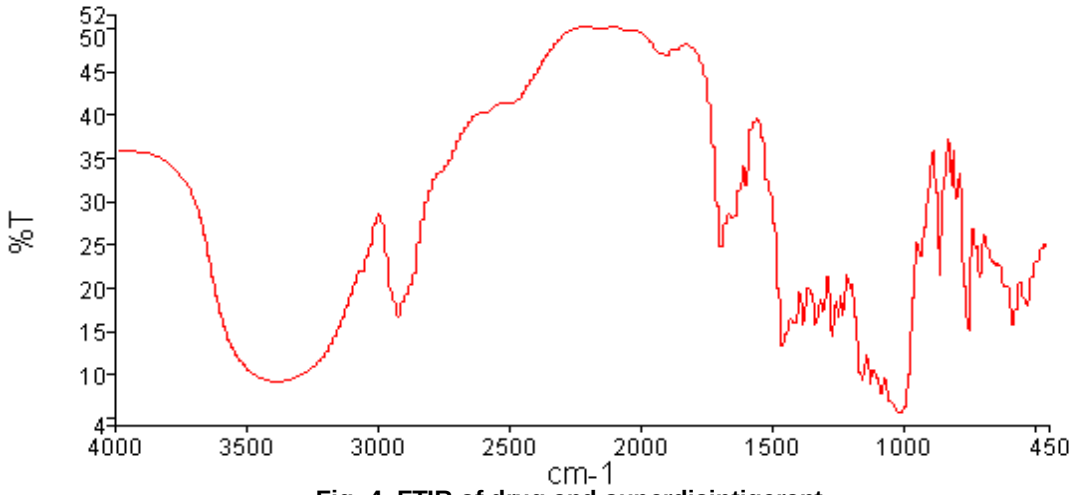

Fig. 4: FTIR of drug and superdisintigerant

CONCLUSION

The release of drug from the F4 formulation was quicker when compared with other formulations .it can be concluded that fast dissolving tablets prepared from Cross caramelose sodium have much better in-vitro dissolution as compared tablet prepared from Crosspovidone and Sodium starch glycolate . The release of formulation F4 was foun to be 99.88% in 30 minutes.

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