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RESEARCH ARTICLE

Formulation and Evaluation of Telmisartan Oral Films

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ABSTRACT

Fast disintegrating oral systems are designed to provide rapid onset of action within a minute without need of water, swallowing or chewing. Telmisartan is an anti-hypertensive agent which is having biological half life of 24 hrs. In order to attain immediate action, Telmisartan oral films were prepared by Solvent casting method using various combinations of polymers and plasticizers. For the present study HPMC E5, Sodium alginate, Gelatin and Maltodextrin were used as polymers and propylene glycol and glycerine were used as plasticizers. Empty films were prepared and evaluated for various physico-chemical properties for selection of suitable polymer and plasticizer combination. Then, drug loaded films were prepared with five selected optimized formulations and evaluated for various parameters. All five formulations are colourless, homogenous and transparent. Among all the formulations , HPMC E5 and propylene glycol combination films showed good results for all the evaluation parameters. Among the five formulations FT1 gave acceptable results like disintegration time of 32 sec which is less than 1 min, dissolving time of 44 sec with maximum drug content of 97.5±0.31 and in-vitro drug release was found to be 98.53% within 10 min. Thus, Telmisartan oral disintegrating films containing HPMC E5 will be a promising drug delivery for immediate drug release in the treatment of hypertension.

Key words: Oral disintegrating films, Telmisartan, Disintegration time, Sodium alginate, HPMC E5.

ARTICLE INFO

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CONTENTS

1. Introduction

The most common and popular route of drug delivery is oral route of drug administration but effectiveness of certain drugs get reduced due to First pass metabolism, drug degradation in variable pH condition of gastrointestinal tract. In order to improve the efficacy of such drugs,

Research and developments has evolved to work out the reconsideration of their delivery strategies. One of such methods is the concept of mouth dissolving drug delivery system. Oral dissolving film has proved its significance due to availability in various size and shape. They provide several advantages such as administration without water, convenience of dosing and rapid onset of action. Their large surface area offers easy disintegration. Oral fast disintegrating films are the solid dosage forms which dissolve or disintegrate quickly in the saliva of oral cavity that result in the formation of solution without the need of water. They are thin elegant films made up of edible, water soluble polymers. Telmisartan, a water insoluble drug, is an angiotensin II receptor antagonist mainly used to treat Hypertension**.**Telmisartan oral fast disintegrating films were prepared by solvent casting method and evaluated for colour, appearance, homogeneity, transparency, folding endurance, thickness, disintegration, drug content and *in-vitro* dissolution studies.

2. Materials and Methods

Telmisartan was obtained from HETERO Drugs ,Vizag, polymers like HPMC E5,Sodium alginate, Maltodextrin, Gelatin were obtained from Sdfcl Fine Ltd. and Di-methyl formamide was procured as gift sample from Molichem Fine Ltd.

Pre-formulation studies

λ_{max} of Telmisartan:

The λ_{max} of Telmisartan was determined by UV-Visible Double beam Spectrophotometer. Initially, the baseline was scanned using suitable solvent like DMF at 200-400 nm. Range. Then the drug solution of 10 mcg/ml. was prepared by using DMF and scanned for maximum absorbance by using UV-Visible Double beam Spectrophotometer.

Standard curve of Telmisartan:

Initially stock solution of 100 mg. in 100 ml. was prepared .Solutions of concentrations ranging from 2 to 10 µg/ml. were prepared from this stock solution using phosphate buffer pH 6.8 and absorbance was measured for each solution at λ_{max} of 300 nm UV visible spectrophotometer and graph was plotted for absorbance versus concentration of Telmisartan.

Determination of Melting point:

Melting point is a simple and rapid method of estimation of purity of a substance. Melting point of Telmisartan is checked by placing the sample in glass capillary tube and heated using melting point apparatus like this an average of three trials were taken.

Fourier Transform Infrared Spectroscopic (FTIR) Analysis:

The FTIR spectrum of Telmisartan and formulation blend were studied by using FTIR Spectrophotometer (Bruker) using the KBr disc method. The scanning range was 400 to 4000 cm^{-1}.

Preparation of empty oral disintegration films:

Oral disintegrating films were prepared by solvent casting method. In this method, the polymer was mixed with 3/4 th volume of water. Then the plasticizer was added with the remaining volume of water and mixed with the polymer solution with continuous stirring by magnetic stirrer. Then, the drug was dissolved in suitable organic solvent and added to the above mixture with stirring. Then citric acid (20 mg), and sodium starch gkycolate (20 mg) were added. This mixture was poured onto the petri-plates or thin plates with 'O' shaped rings present on it. These contents were transferred into hot air oven and dry for 8-10 hours at 80^0C. The films which are formed should be cut into equal dimensions and packed and labelled properly.

These empty films were further evaluated for various parameters and combination of polymers and plasticizers showing better film consistency were selected for preparation of drug loaded films.

Preparation of Telmisartan oral disintegrating films:

Based on the results obtained from Empty films, HPMC and Sodium alginate were selected as optimum film forming polymers and drug loaded films were prepared with them by various combinations of plasticizers.

Drug loaded oral disintegrating films were also prepared by Solvent casting method as described above by dissolving the drug (Telmisartan) suitable solvent (Di-Methyl Formamide)

Evaluation of Telmisartan oral films

Homogeneity:

All the films with and without drug were evaluated for physical appearance and classified on the basis of Homogeneity and non-homogeneity.

Colour:

The colour of all the prepared films was visually observed to check the uniformity of colour.

Thickness:

Three films of each formulation were taken and their thickness was measured using screw gauge at three different places and the mean thickness of films were calculated and reported.

Folding endurance:

Folding endurance was measured by manual repeated folding of film at same place till it breaks. The number of times the film was folded without breaking is known as the folding endurance value. A strip of 3 x 2 cm diameter was subjected to folding endurance by folding the film in the same place repeatedly several times until a visible crack was observed and the average values are calculated and reported**.**

Surface pH:

The film was placed in a petridish and moistened with 0.5 ml. of distilled water. The pH was noted by bringing the electrode of pH meter in contact with the surface the formulation .

Disintegration time:

A film was placed in the basket of disintegration apparatus, raised and lowered in such a manner that complete up and down movement at a rate to achieve equivalent to 30 times a minute. Time required by the film to achieve no trace of film remaining above the gauze was noted.

Dissolving time:

The dissolving time was determined by placing the film in a beaker containing 50 ml. of phosphate buffer (pH 6.8) . Time required by the film to dissolve completely was noted.

Drug content:

A circular film of 2.5 cm. diameter was cut and placed in a beaker containing 100 ml. of phosphate buffer pH 6.8 solutions. The contents were stirred in magnetic stirrer to dissolve the film and the contents were transferred to 100 ml. volumetric flask. The absorbance of the solution was measured against the corresponding blank solution at 300 nm. As the absorbance noted above 1 mcg/ml.,1 ml. of the stock further diluted to 10 ml. of phosphate buffer solution (pH 6.8) and absorbance was measured at 300 nm.

Dissolution studies:

The *in-vitro* dissolution studies were conducted using dissolution media phosphate buffer (500 ml.) in USP dissolution apparatus at $37+0.5^0$c and at 50 rpm Each film with dimension (2 x 2 cm^2) was submerged into dissolution media samples containing 5 ml. volume were withdrawn at 0,2,5,10,15,20,25 and 30 min. time intervals and filtered through 0.45 micron whatmann filter paper and were analysed spectrophotometrically at 300 nm. To maintain the volume,an equal volumes of fresh dissolution medium, maintained at same temperature was added after withdrawing samples.

3. Results and Discussion

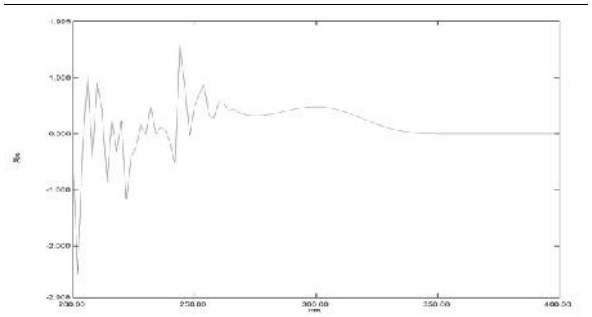

Figure 1: λ_{max} of Telmisartan

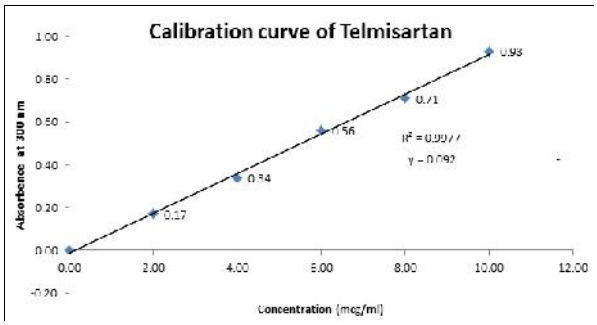

Figure 2: Calibration curve of Telmisartan

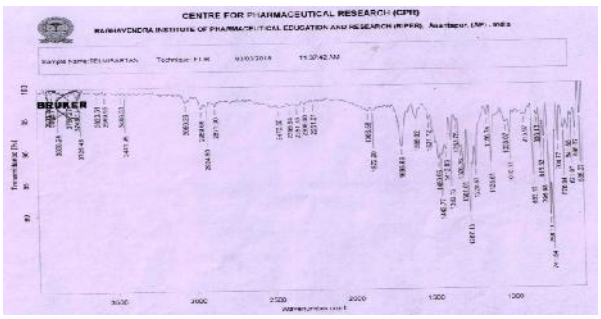

Figure 3: FTIR of Telmisartan

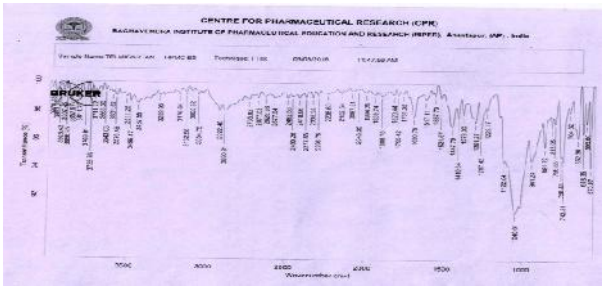

Figure 4:FTIR of Telmisartan-HPMC E5

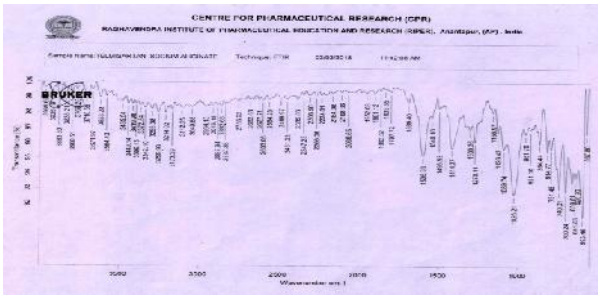

Figure 5:FTIR of Telmisartan-Sodium alginate

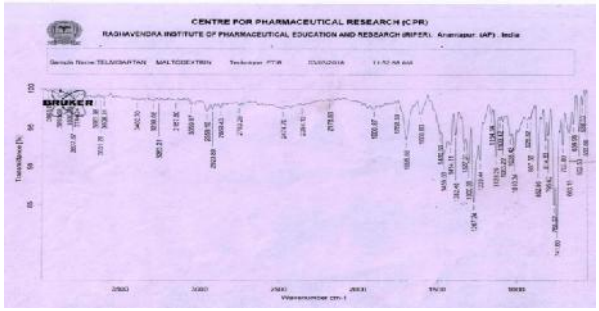

Figure 6: FTIR of Telmisartan-Gelatin

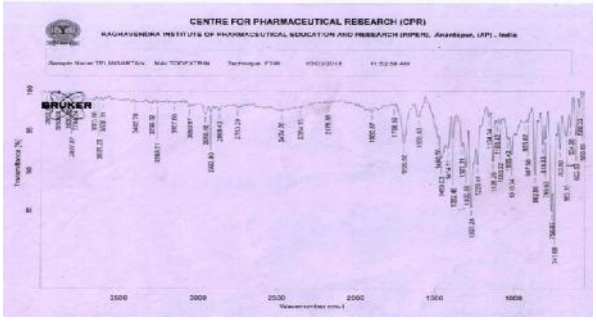

Figure 7: FTIR of Telmisartan-Maltodextrin

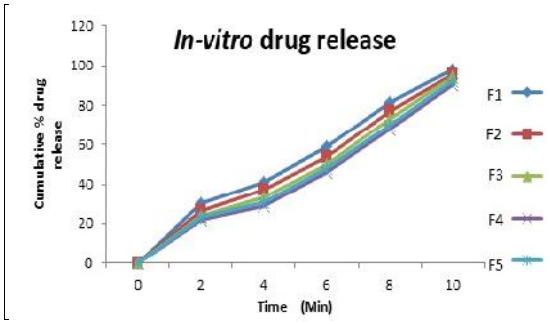

Figure 8: Comparision of in-vitro drug release of formulations FT1-FT5

4. Conclusion

In our work we have formulated nineteen formulations without drug using various natural and synthetic polymers like sodium alginate, gelatin, maltodextrin and hydroxyl propyl methyl cellulose in different combinations of Plasticizers. All 19 formulations have been prepared by solvent casting method & evaluated for their morphological, mechanical *in-vitro* properties. Based on the results obtained we have selected formulation containing HPMC and Sodium alginate as optimised formulations. After optimisation we have formulated 5 films containing Telmisartan with different concentrations of HPMC and Sodium alginate by solvent casting method and evaluated for morphological properties, mechanical properties and *in-vitro* properties. All five formulations were colourless, homogenous and transparent. In the evaluation of mechanical properties the thickness of all 5 formulations were found to be less than or around one mm and folding endurance was also found to be good. From the evaluation of *invitro* properties, the pH of all five formulations found to between 6.4-6.9 which is the pH of oral mucosa. In evaluation of disintegration time all the films were disintegrated within 1 min. In drug content evaluation FT 1 has maximum drug content of 97.5±0.31 %. *Invitro* drug dissolution studies the FT 1 shown 98.53±0.70% of drug release within 30 min.

Table 1: λmax of Telmisartan

S.No.	λ_{max}	Absorbance
1	300 nm.	0.478

Table 2: Calibration data of Telmisartan

Conc.(mcg/ml)	Absorbance
0	0
2	0.175
4	0.343
6	0.561
8	0.712
10	0.934

Table 3: Melting point of Telmisartan

S.No.	Trails	M.Pt.(^{0} C)
1	Trail-1	262
2	Trail-2	265
3	Trail-3	259
Average		**262**

Table 4: Functional groups and associated wave numbers of FTIR spectra of Telmisartan

Functional group	Observed wave number (cm^{-1})					
	Telmisartan	**Telmisartan and sodium alginate**	**Telmisartan and HPMC E5**	**Telmisartan and gelatin**	**Telmisartan and Maltodextrin**	**Wave number range (cm^{-1})**
C=C [Ar]	1460.95	1495.53	1410.64	1457.32	1459.03	1400-1600
C-H [Ar]	3059.29	3049.88	3054.75	3060.46	3059.97	3000-3100
C-N [Ar]	1267.13	1270.11	1122.04	1267.46	1267.24	1080-1360
C-H [Ali]	2924.50	2863.66	2890.81	2930.16	2923.80	2850-3000
C=O	1695.63	1689.40	1690.78	1695.05	1695.56	1670-1820
OH	3569.55	3584.43	3485.47	3543.46	3263.21	3200-3600

Table 5: Formulation of Telmisartan oral films

Ingredients	FT1	FT2	FT3	FT4	FT5
TLM (g)	20	20	20	20	20
DMF (ml)	5	5	5	5	5
HPMC E5 (g)	1.5	2.5	7.5	7.5	-
Sodium alginate (g)	-	-	-	-	1.5
Propylene glycol(ml)	-	1	5	1	-
Glycerine (ml)	5	-	-	-	5
Ethanol (ml)	10	-	-	-	20
Water (ml)	10	100	100	100	20

Table 6: Formulation of empty oral disintegrating films

Formulation	HPMC (mg)	Sodium alginate (mg)	Gelatin (mg)	Malto-dextrin (mg)	Propylene glycol (ml)	Glycer-ine (ml)	Ethanol (ml)	Water (ml)
F1	1.5	-	-	-	1	-	-	100
F2	1.5	-	-	-	-	5	20	20
F3	2.5	-	-	-	1	-	-	100
F4	2.5	-	-	-	-	5	25	25
F5	5	-	-	-	1	-	-	100
F6	5	-	-	-	-	5	30	30
F7	7.5	-	-	-	1	-	-	100
F8	7.5	-	-	-	5	-	-	100
F9	-	1.5	-	-	-	5	20	20
F10	-	2.5	-	-	-	5	25	25
F11	-	5		-	-	5	30	30
F12	-	-	1.5	-	1	-	-	100
F13	-	-	1.5	-	-	5	20	20
F14	-	-	2.5	-	1	-	-	100
F15	-	-	2.5	-	-	5	25	25
F16	-	-	-	1.5	1	-	-	100
F17	-	-	-	1.5	-	5	20	20
F18	-	-	-	2.5	1	-	-	100
F19				2.5	-	5	25	25

Table 7: Morphological and Mechanical properties of Telmisartan Oral Films

Formulation code	Colour	Homogeneity	Transparency	Thickness (mm)	Folding endurance
FT1	Colourless	Homogenous	Transparent	0.7	52
FT 2	Colourless	Homogenous	Transparent	0.9	49
FT 3	Colourless	Homogenous	Transparent	1.1	55
FT 4	Colourless	Homogenous	Transparent	0.8	60
FT 5	Colourless	Homogenous	Transparent	1.1	48

Table 8: In-vitro properties of films containing drug

Formulation code	Surface pH	Disintegration time (sec)	Dissolving Time (sec)	Drug content (%)
FT 1	6.7	32	44	97.5±0.31
FT 2	6.9	38	49	96.7±0.24
FT 3	6.9	36	49	94.8±0.53
FT 4	6.6	44	54	91.4±0.61
FT 5	6.5	49	69	93.4±0.12

Table 9: Comparision of in-vitro drug release of formulations FT1-FT5

Time (min)	CUMULATIVE PERCENTAGE DRUG RELEASE(%)				
	FT 1	**FT 2**	**FT 3**	**FT 4**	**FT 5**
0	0	0	0	0	0
2	30.51±0.66	26.54±0.45	24.66±0.75	22.45±0.32	23.51±0.46
4	41.47±0.23	37.12±0.49	33.23±0.26	29.37±0.66	31.26±0.14
6	59.44±0.45	54.98±0.78	50.14±0.56	46.36±0.41	48.47±0.71
8	81.56± 0.18	77.33±0.64	73.71±0.47	68.59±0.96	70.48±0.55
10	98.53±0.70	95.89±0.56	94.22±0.69	90±0.84	92.11±0.64

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