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Research **Article**

FORMULATION, DEVELOPMENT AND IN-VITRO EVALUATION OF TELMISARTAN USING POLYMERS IN FLOATING DRUG DELIVERY SYSTEM

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ABSTRACT:

The therapeutic effectiveness of Telmisartan an (ARB) angiotensin II receptor blocker that is often used to treatment of hypertension is limited by its low bioavailability (42–58%) and water solubility is poor. Patient compliance is decreased by the frequent dosage required by conventional formulations. To overcome these obstacles a floating drug delivery system (FDDS) that used natural polymers was created to improve telmisartan's solubility, prolonged release and stomach retention. Natural polymers with gel-forming, biodegradable and biocompatible qualities such as xanthan gum, HPMC and PEO were used. Direct compression was used to create the formulations (F1–F9) which were then assessed for buoyancy, in vitro drug release and physicochemical characteristics. The compatibility of telmisartan with excipients were evaluated by FTIR and DSC analyses. The tablets' hardness, friability and flow characteristics were all satisfactory. According to buoyancy studies total floating periods ranged from 9.5 to 11.5 hrs with floating lag times ranging from 38 to 55 seconds. Studies on drug release in vitro showed sustained release for 12 hrs with the best release patterns being shown by F3 and F9. The study comes to the conclusion that Floating Drug Delivery System (FDDS) of telmisartan utilizing polymers can increase patient compliance, decrease the frequency of dose and improve bioavailability providing a viable strategy for managing hypertension.

Keywords: Telmisartan, Floating Drug Delivery System (FDDS), Polymers, Sustained release, Bioavailability enhancement.

INTRODUCTION

Telmisartan an angiotensin II receptor blocker (ARB) is frequently recommended to treat hypertension a condition that is a global health problem. Poor water solubility and low bioavailability (about 42–58%) which are typical problems for BCS Class II medications like Telmisartan restrict its therapeutic effectiveness. The Conventional oral formulations can lead to frequent dosing and reduced patient compliance since they are unable to provide sustained medication release. In an attempt to get beyond these limitations advanced drug delivery systems like floating drug delivery systems (FDDS) have attracted a lot of interest. Since the upper gastrointestinal tract is where telmisartan is mostly absorbed FDDS are designed to lengthen the stomach retention period, facilitating improved absorption and longer drug release in that area. There are a number of benefits to using natural polymers in FDDS including cost-effectiveness, biocompatibility and biodegradability. Because of their capacity to create gels regulate medication release and offer buoyancy polymers including chitosan, sodium alginate, guar gum and xanthan gum are being investigated extensively. These polymers produce a low-density system that floats atop stomach juices when mixed with gas-forming chemicals such as sodium bicarbonate guaranteeing extended contact with the absorption site. This method improves patient adherence by lowering dosage frequency, increasing the solubility and bioavailability of medications that are poorly soluble in water such as telmisartan. Primary goal of this effort is to create and evaluate in vitro a floating

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drug delivery system for telmisartan using natural polymers. The formulation aims for improved physicochemical properties, extended drug release, and optimized buoyancy. The goal of this research is to develop a gastro-retentive system that uses the unique properties of natural polymers to overcome the shortcomings of conventional Telmisartan formulation, offering a practical means of effectively treating hypertension. In vitro evaluation will include buoyancy studies, drug release kinetics, and physicochemical characterization to ensure the formulation's stability and efficacy.

MATERIALS AND METHODS

Materials

Aurobindo Drugs sent a gift sample of telmisartan, while Colorcon provided HPMC, PEO, PVPK30, and xanthum gum. Magnesium stearate, Evonik India, Avicel from FMC Biopolymer Mumbai, NaHco3 from SD Fine Chemicals Mumbai, and Talc from SD Fine Chemicals.

Calculating Telmisartan's λ Max in 0.1N HCL

A 1000µg/ml ppm concentrated stock solution was obtained by weighing 50 mg of the model drug, dissolving it in 50 ml of 0.1N HCL, and then adding more 0.1N HCL to reach a volume of 50 moles. Dilution 1: A concentrated solution containing 10 µg/ml was obtained by diluting 1 ml of the working standard solution with 100 ml of 0.1NHcl. The relevant scan spectrum curve was recorded when this solution was scanned at wavelengths between 190 and 400 nm. λ max is the wavelength that corresponds to the maximal absorption.

Studies of compatibility (FTIR spectroscopy)

Bruker FTIR Germany (Alpha T) was used to assess the compatibility of the additions and the pure medication. After placing the powdered sample over a yellow ZnSe crystal, the spectra were captured in the wave number range of 4000 cm-1 to 400 cm-1.

Calibration curve of Model drug in 0.1N HCL:

A 1000µg/ml ppm concentrated stock solution was obtained by weighing 50 mg of the model drug dissolving it in 50 ml of 0.1N HCL and then adding more 0.1N HCL to reach a volume of 50 ml. Various concentrations were made from the stock solution. Using 0.1N HCl as a blank the absorbance of the samples was measured at 248 nm using a UV spectrophotometer.

Calorimetry using differential scanning (DSC)

Both physical mixtures of pharmaceuticals with specific polymers and pure medications were subjected to DSC analysis. A 10 mg sample was heated in an aluminium (Al) pan at 30 to 450°C while nitrogen passed through it at a rate of 50 mL per minute (Mettler-Toledo STARSW 9.20, USA).

Formulation of gastro retentive floating tablets

The General Methodology listed below was used to create the matrix tablets:

After precisely weighing each component and co-sifting it through a #40 sieve it was mixed for five minutes in a Poly Bag. The aforementioned granules were lubricated using talc and magnesium stearate that had gone through a #60 sieve. A 16-station tablet compression machine with an average hardness of 4.0KP was then used to compress the final mix into tablets using a 9mm die.

Table 1: Telmisartan floating matrix tablet preparation in several batches

Formula	TELMISARTAN (mg)	XANTHUM GUM (mg)	PEO WSR 303 (mg)	HPMC K4M (mg)	NAHCO3 (mg)	PVPK30 (mg)	Mg STEARATE (mg)	TALC (mg)
F1	40	40	-	-	20	15	1	1
F2	40	60	-	-	20	15	1	1
F3	40	80	-	-	20	15	1	1
F4	40	-	40	-	20	15	1	1
F5	40	-	60	-	20	15	1	1
F6	40	-	80	-	20	15	1	1
F7	40	-	-	40	20	15	1	1
F8	40	-	-	60	20	15	1	1
F9	40	-	-	80	20	15	1	1

RESULTS AND DISCUSSION

Analytical Method: Telmisartan drug standard calibration curve in 0.1N HCl

Using 0.1N HCl as a blank, the absorbance of the solution was measured at 248 nm using a UV spectrophotometer. Tablets 20 displays the values. A plot of absorbance against concentration showed that Beer's law was being followed.

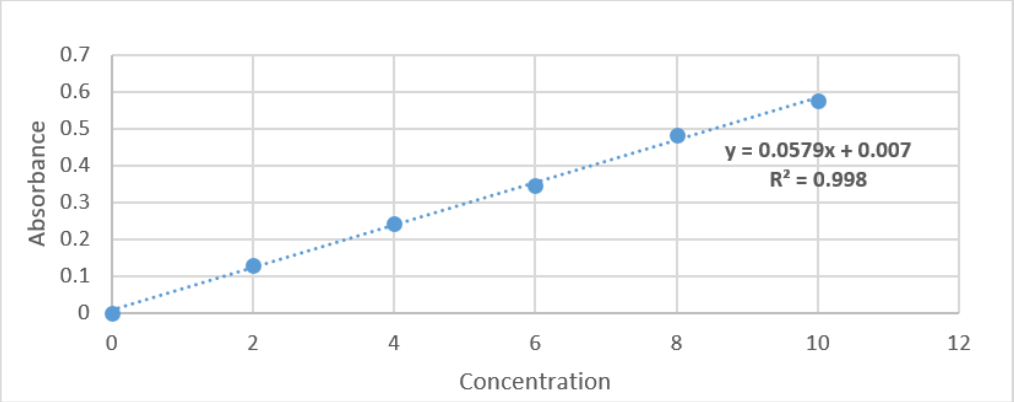

Fig 1: Calibration curve of Telmisartan in 0.1N HCl

Compatibility studies – FTIR

The FTIR data clearly showed no obvious interactions between the medicine and excipients. Telmisartan and particular polymers were, therefore, thought to be compatible. Figures 2, shows FTIR of pure drug.

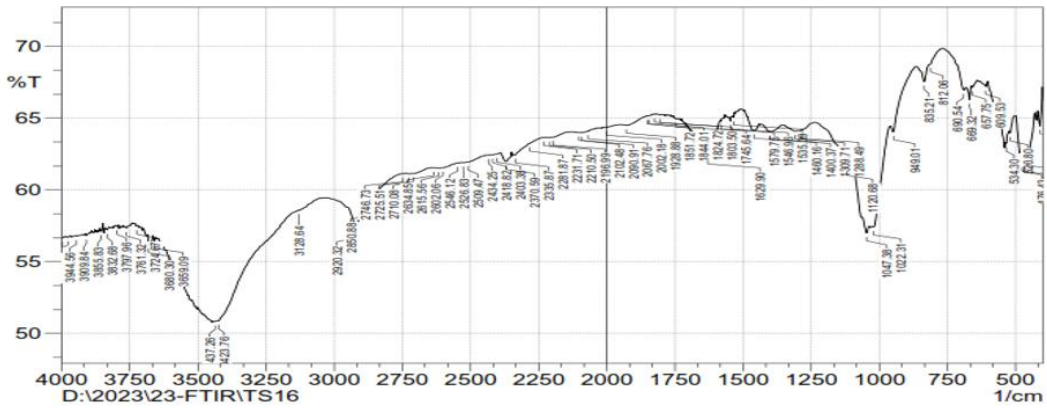

Fig 2: FTIR of Telmisartan pure drug

Compatibility studies – DSC

A noticeable endothermic peak was seen at 78 degrees Celsius indicating that Telmisartan was melting as a result of a temperature-induced phase change. The phase transition started at 269 °C and ended at 272 °C (Fig (3))

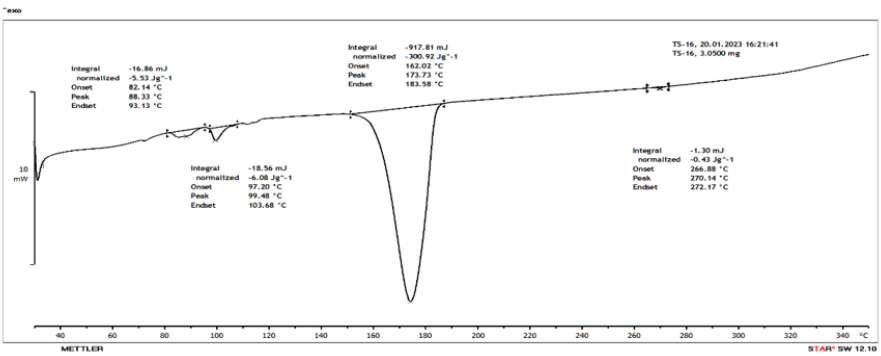

Fig 3: DSC of Telmisartan pure drug

Table 2: Powder Flow Properties of Formulations (F1–F9)

Formulation	Angle of Repose (°)	Bulk Density (g/cm³)	Tapped Density (g/cm³)	Carr's Index (%)	Hausner's Ratio
F1	28.5	0.45	0.52	13.5	1.16
F2	29.0	0.46	0.53	13.2	1.15
F3	29.2	0.47	0.54	12.9	1.15
F4	28.8	0.44	0.51	13.7	1.16
F5	29.1	0.45	0.52	13.5	1.16
F6	29.3	0.46	0.53	13.2	1.15
F7	28.7	0.44	0.51	13.7	1.16
F8	29.0	0.45	0.52	13.5	1.16
F9	29.2	0.46	0.53	13.2	1.15

Table 3: Post-Compression Study Results of Formulations (F1–F9)

Formulation	Weight Variation (%)	Friability (%)	Thickness (mm)	% Drug Content	Hardness (kg/cm²)
F1	2.1	0.45	3.2	98.5	5.2
F2	1.9	0.42	3.1	99.2	5.4
F3	2.0	0.43	3.2	98.8	5.3
F4	2.2	0.46	3.3	97.9	5.1
F5	1.8	0.41	3.1	99.5	5.5
F6	2.0	0.44	3.2	98.7	5.2
F7	2.1	0.45	3.3	98.2	5.0
F8	1.9	0.43	3.1	99.0	5.4
F9	2.0	0.42	3.2	98.6	5.3

Table 4: In Vitro Buoyancy Study Results of Formulations (F1–F9)

Formulation	Floating Lag Time (FLT) (seconds)	Total Floating Time (TFT) (hours)
F1	45	10.5
F2	40	11.0
F3	38	11.5
F4	50	10.0
F5	42	10.8
F6	39	11.2
F7	55	9.5
F8	48	10.2
F9	43	10.7

In Vitro Drug Release Studies

Table 5: Cumulative Drug Release (%) of Formulations (F1–F9)

Time (hours)	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	12.5	11.8	10.5	13.2	12.0	11.0	14.0	13.5	12.8
2	25.0	23.5	21.0	26.0	24.5	22.0	27.5	26.0	24.8
4	45.0	42.5	40.0	47.0	44.5	41.0	49.0	47.5	45.8
6	65.0	62.5	60.0	67.0	64.5	61.0	69.0	67.5	65.8
8	80.0	78.5	75.0	82.0	79.5	76.0	84.0	82.5	80.8
10	92.0	90.5	88.0	93.0	91.5	89.0	94.0	93.5	92.8
12	98.5	97.0	95.0	99.0	98.0	96.0	99.5	99.0	98.8

CONCLUSION

The study effectively addressed Telmisartan's low bioavailability and poor solubility by creating a floating drug delivery system (FDDS) with using polymers such xanthan gum, HPMC and PEO. Direct compression was used to create formulations (F1–F9) which were then assessed for buoyancy, physicochemical characteristics and in vitro drug release. There were no conflicts between Telmisartan and the excipients according to compatibility tests (FTIR and DSC). The tablets flow, friability and hardness were all excellent. According to buoyancy experiments total floating periods ranged from 9.5 to 11.5 hours with floating lag times of 38 to 55 seconds guaranteeing extended stomach retention. Research on drug release in vitro showed sustained release for 12 hours with optimum release profiles for F3 and F9 being 95% and 98.8% respectively. Polymers decreased the frequency of doses improving medication solubility, bioavailability and patient compliance. The use of Floating Drug delivery system (FDDS) presents a viable methods for enhancing Telmisartan's therapeutic effectiveness in the treatment of hypertension. It is advised to do more in vivo research to confirm these results.

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