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# FORMULATION AND *IN VITRO* EVALUATION OF FLOATING TABLETS OF FENUGREEK MUCILAGE AS NATURAL BINDER USING TELMISARTAN AS A MODEL DRUG

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## ABSTRACT

The present study was carried out with an objective of preparation and in vitro evaluation of fenugreek mucilage floating tablets using Telmisartan as a model drug incorporated hydroxyl propyl methyl cellulose of two different grades were employed. Telmisartan (TEL) is a selective angiotensin II receptor blocker used in the management of cardiovascular disorders. It is a class II drug according to biopharmaceutics classification system with poor solubility and high permeability. Owing to its hydrophobicity, TEL demonstrates low dissolution behavior in gastro-intestinal (GIT) media ensuing deprived absorption, and later poor bioavailability. The Gastro Retentive Floating Tablets (GRFT) were formulated by means of hydroxy propyl methyl cellulose (HPMC) and naturally extracted binder from the seeds of Trigonella foenum (Fenugreek). Three batches were formulated by using two different grades of HPMC namely K15 and E50. These prepared formulas were examined for Drug-excipient incompatibility studies by FT-IR, angle of repose, Carr's Index (CI), Hardness, Weight variation, Floating Lag Time (FLT), Floating Duration (FD) and dissolution profile. It was concluded that by using HPMC K15 gives the better bioavailability when compared with the HPMC E50 and combination of both grades as a floating drug delivery

system of Telmisartan.

**Keywords:** Gastro Retentive Floating Tablets (GRFT), HPMC, Trigonella foenum (Fenugreek)

## INTRODUCTION

Drug get absorbed in the initial part of GIT, drugs that are less soluble or those degrade in the alkaline PH may be benefited from prolonged gastric retention. Prolonged gastric retention increases bioavailability, decreases wastage of drugs, increases solubility of drugs. Drugs that have narrow absorption window in the gastrointestinal tract will have poor absorption for which gastro retentive drug delivery systems (GRDDS) offer the advantage in prolonging the gastric emptying time. To formulate a successful stomach specific or GRDDS, several techniques like low density, high density, and raft systems are employed by incorporating alginate gels, bio adhesive or mucoadhesive systems, super porous hydrogels, magnetic Systems and in-situ floating gels.

Angiotensin-II is a potent vasoconstrictor (blood vessels to tighten) and is involved in the synthesis and release of aldosterone. Losartan binds to Angiotension II receptor subclass of AT1 and inhibits Angiotension II and leading to a vasodilatory effect and decrease in peripheral vascular resistance and B.P. As a result, losartan relaxes the blood vessels. A lower blood pressure will increase the supply of the blood and oxygen to the heart.

Angiotensin-II receptors are present in at least 4 subclasses include $AT_1$,$AT_2$, $AT_3$ and $AT_4$. (These G-protein coupled receptors and are responsible for signal transduction of the hormone). $AT_1$ receptors are managing specific cardiovascular diseases which present in brain, vascular, renal, hepatic , adrenal and myocardial tissues and mediates CNS, cardiovascular and renal effects of the Angiotensin II. All currently available ARBs are 10,000 times more selective for ($AT_1$) receptor subtype. Candesartan and Olmesartan have Greatest affinity. Irbesartan and eprosartan have some what lower affinity. Telmisartan, Valsartan and Losartan have the lowest affinity.

## MATERIALS AND METHODS

Telmisartan was used as an active ingredient. HPMC E50 & HPMC K15 were used as polymers. Fenugreek mucilage was used as a natural binder. Sodium bicarbonate was used as a gas generating agent. Other ingredients used in the formulation were Magnesium stearate as lubricant and talc as glidant. All the materials used in the formulation were purchased from Sigma Aldrich and all are of analytical grade.

**DETERMINATION OF $\lambda_{max}$ AND CALIBRATION CURVE OF TELMISARTAN**

A solution of 400 µg/ml of Telmisartan in a buffer solution ($P^H$=1.2) of 0.1 N HCl was made and the λmax of the drug was determined using UV visible spectrophotometer scanner (Range: 200-400 nm). A calibration curve of Telmisartan was constructed by preparing serial dilutions of different concentrations (2, 4, 6, 8, 10, 12 and 14 µg/ml) of TEL at the λmax of the drug, the absorbance was measured and plotted against the respective concentrations.

**Preparation of Telmisartan floating tablets by wet granulation method**

The composition of different formulations of Telmisartan was mentioned in the table. Telmisartan and all other ingredients were weighed and sieved separately and mixed using fenugreek mucilage as a binder and made into soft dough and then wet screening was done using sieve no.10 and then granules were dried in a hot air oven and then dried granules were sieved using sieve no.12 and weighed quantities of lubricant and talc was added and mixed well and compressed into tablets.

| S.No | Name of the product | Quantity/Tablet | Use |
|---|---|---|---|
| 1 | Telmisartan | 40mg | Drug |
| 2 | Hydroxypropyl methyl cellulose (HPMC) of two grades | 350mg | Polymer |
| 3 | Fenugreek gum | 10mg | Binder |
| 4 | Sodium bicarbonate | 85mg | Gas generating agent |
| 5 | Talc | 10mg | Glidant |
| 6 | Magnesium stearate | 5mg | Lubricant |

**Table 01: Formula to prepare Telmisartan Floating tablets**

## Evaluation of Formulated Telmisartan Floating Tablets

### Determination of Organoleptic Properties:

The organoleptic properties of formulated tablets such as colour, odour and texture was determined by visual inspection of tablets

### Determination of floating lag time and floating duration

Floating lag time (FLT) can broadly be defined as the duration interval of introducing the tablet into the dissolution media and its floatation to the surface of that media; while period up to which the tablet hangs on the surface of dissolution mixture was termed as floating duration (FD). These parameters were calculated by introducing the tablets in a beaker (100 mL) containing 0.1N HCl. The mixture was kept in quiet condition and the temperature was stored $37^0$ C.

### Hardness

Hardness indicates the ability to withstand mechanical shocks while handling. The hardnessof the tablets was determined using Monsanto hardness tester. It is expressed in $Kg/cm^2$. Five tablets were randomly picked, and the hardness of the tablets was determined.

### Friability test:

The friability of the tablets was determined by using Roche friabilator.

It is expressed in percentage%. Twenty tablets were initially weighed (Wi) and transferred into friabilator. The friabilator was operated at 25rpm for 4min or run up to 100 revolutions. The tablets were weighed again (Wr). The %friability was then calculated by:

$$\%friability = W_1 - W_2/W_1 * 100$$

### Uniformity of weight (weight variation test):

Any variation in the weight of tablet (for any reason) leads to either under medication or overdose. So, every tablet in each batch should have a uniform weight. Twenty tablets were selected randomly from each batch and weighed individually to check for weight variation. A little variation was allowed in the weight of a tablet according to US pharmacopoeia. The following percentage deviation in weight variation was allowed.

### Uniformity of content:

Twenty tablets were weighed and transferred into a mortar, crushed them into fine powder and mixed well. The sample powder equivalent to 250 mg drug was accurately weighed and transferred to a 100 ml volumetric flask. About 50 ml phosphate buffer of $p^H$ 6.8 was added and sonicated to dissolve. The

volume was made up to the mark with diluent and mixed well. 1 ml of this solution was diluted to 100 ml with the same diluent and mixed. Then the amount of drug was determined by measuring the absorbance of the solution using UV –visible spectrophotometer.

**Swelling index:**

Swelling index of fenugreek powder was studied in 0.1 N HCl. 1 gm of sample was added to 10 ml of 0.1 N HCl . The cylinder was shaken vigorously for 10 min and allowed to stand for 24 hrs. Swelling capacity was expressed as;

**Swelling capacity = (%v/v) = [$X_V/X_i$] *100**

Where, $X_V$ is the final volume occupied by swollen material after 24 hrs and $X_I$ denotes the initial volume of the powder gum in graduated measuring cylinder.

*In-vitro* drug release study:

| | | |
|---|---|---|
| Apparatus | : | Dissolution apparatus USP type II (paddle) |
| Medium | : | 1.2 $P^H$ HCl buffer |
| Volume | : | 900 ml |
| Speed | : | 100 ml |
| Time intervals | : | 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4...hours |
| Temperature | : | 37± $2^0$ C |
| Equipment | : | UV-Visible spectrophotometer |
| Wave length | : | 205 nm |

**Dissolution medium preparation:**

Placed 50.0ml of the 0.2M potassium chloride in a 200 ml volumetric flask and added 85ml specified volume of 0.2 M hydrochloride acid and then added water to make up the volume.

**Sample preparation:**

The dissolution test apparatus was kept as per the above conditions. One tablet was placed in each dissolution bowl and the apparatus was run. After specified time interval, 5ml of liquid was withdrawn from the zone midway between the top of rotating paddle and surface of dissolution medium and 1cm away from the wall of jar. The solution was filtered through 0.45 membrane filter, rejecting the first few ml of the filtrate into a separate test tube. Further 1ml was diluted to 10 ml

with the dissolution medium. Again 1ml of resulting solution was diluted to 10 ml with dissolution medium and mixed well.

**Procedure:** The instrument was switched on and stabilized. The instrument was made up to zero and then the absorbance of blank and sample was measured at 273nm using the dissolution medium as blank

**Formula:**

The % drug release of Telmisartan present in the tablet was calculated by using theformula:

**Amount dissolved = Absorbance obtained* amount of dissolution * diluted factor*standard concentration / Standard Absorbance * 1000**

**Percentage dissolved = Amount dissolved / Total drug * 100**

**RESULT AND DISCUSSION:**

**Calibration Curve of Telmisartan using $P^H$-1.2 Hydrochloric Acid Buffer**

| Data | Result |
|---|---|
| **Medium** | 0.1 N HCl |
| **λmax** | 205nm |
| **$R^2$** | 0.9957 |

**Table 02: Standard curve of $P^H$-1.2 HCl buffer**

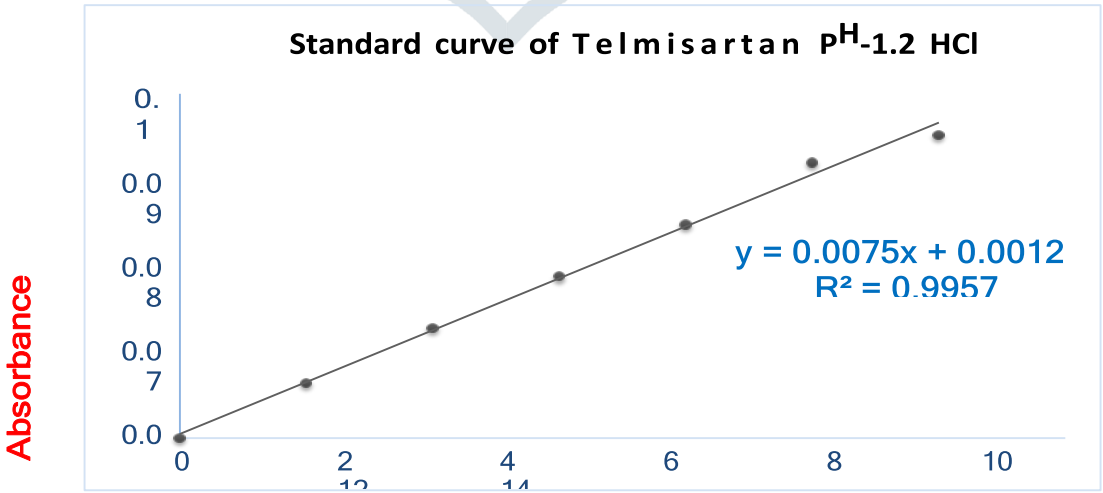

**Fig.01 Standard calibration curve of Telmisartan in 0.1 N HCl**

**Evaluation of Telmisartan floating tablet:**

| Formulation | Hardness ($kg/cm^2$) | Weight variation (mg) | Friability (%) | Drug content (%) | Floating lag time (sec) | Total floating time (hrs) |
|---|---|---|---|---|---|---|
| **F1 (With HPMC K15)** | 4.2 | -3 | 0.7 | 100.56 | 38 | >18 |
| **F2 (With HPMC E50)** | 4.2 | -5 | 0.7 | 100.21 | 33 | >18 |
| **F3(HPMC K15+ HPMC E50)** | 5.2 | -5 | 0.7 | 99.85 | 21 | >18 |

**Table 03: Evaluation Parameters of Telmisartan floating tablets**

***In vitro* drug release studies:**

| Time (Hrs) | % Drug Release | | | |
|---|---|---|---|---|
| | Conventional Telmisartan Tablets | With HPMC K15 | With HPMC E50 | HPMC K15+ HPMC E50 |
| 0 | 0 | 0 | 0 | 0 |
| 0.25 | 0.42 | 0.22 | 0.18 | 0.21 |
| 0.5 | 0.89 | 0.66 | 0.52 | 0.58 |
| 0.75 | 1.46 | 0.93 | 0.86 | 0.92 |
| 1 | 2.01 | 1.06 | 1.03 | 1.06 |
| 1.5 | 2.78 | 1.83 | 1.53 | 1.77 |
| 2 | 3.96 | 2.75 | 2.74 | 2.77 |
| 2.5 | 4.88 | 3.51 | 3.22 | 3.47 |
| 3 | 5.47 | 4.66 | 4.44 | 4.52 |
| 3.5 | 6.15 | 5.93 | 5.53 | 5.67 |
| 4 | 6.93 | 7.05 | 6.87 | 6.94 |
| 4.5 | 7.84 | 8.17 | 7.95 | 8.09 |
| 5 | 8.48 | 9.24 | 8.74 | 9.06 |
| 5.5 | 9.05 | 10.34 | 9.35 | 9.86 |
| 6 | 9.94 | 11.55 | 10.03 | 10.25 |

**Table 04: *In vitro* drug release of Telmisartan floating tablets**

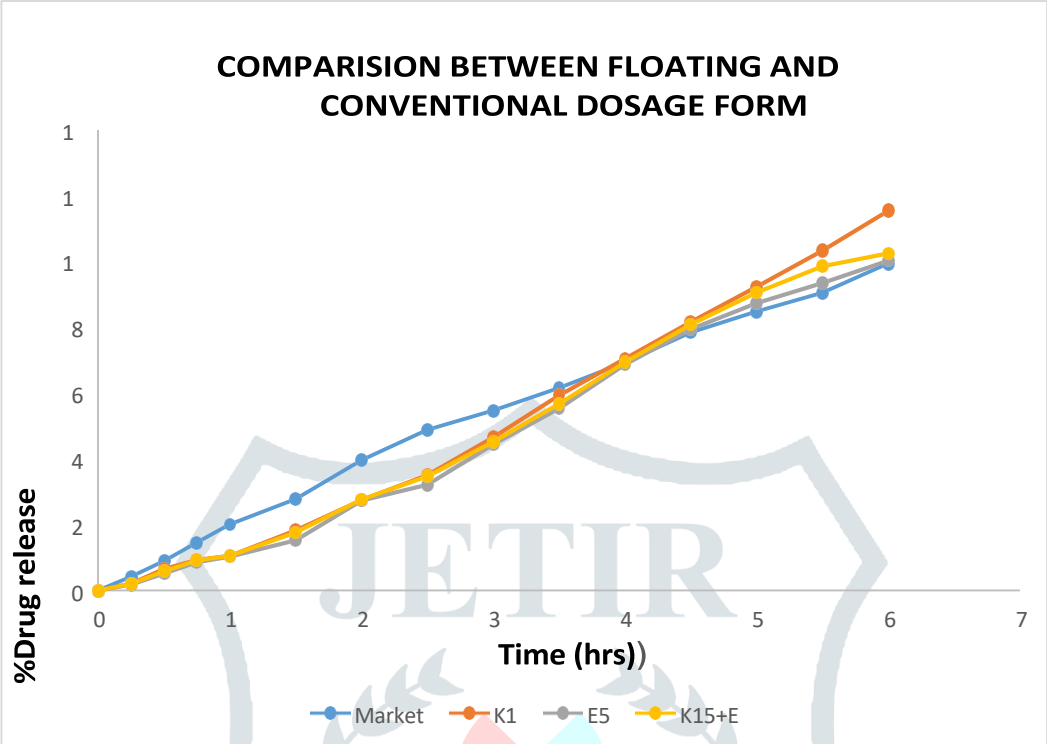


**Fig.02 Comparison between floating Tablets and conventional dosage form**

## DISCUSSIONS:

### CALIBRATION CURVE:

The absorbance values and standard plot was shown in Table-02. From these results, it was found that there exists a decent correlation between the concentration and absorbance and the regression co efficient value was found to be 0.9957.

### Studies on Telmisartan floating tablets formulated with HPMC $K_{15}$:

Floating tablets of Telmisartan was prepared by using HPMC grade $K_{15}$. three batches were formulated using same concentration of HPMC and other ingredients. The Composition of the formulation was shown in Table 01. The floating tablets were formulated using fenugreek seed mucilage by wet granulation method.

The floating tablets are further evaluated for post-compression parameters like hardness, friability, weight variation, drug content uniformity, floating lag time and total floating time shown in the Table 03. The average hardness of all the formulations ranges between 4.2-4.5 ($kg/cm^2$). All the tablets passed the weight variation test as the % weight variation was within the pharmacopeia limits of ±5. The tablets satisfied friability requirement, as the % friability values were less than 1%. The drug content estimations showed values ranges between 99.98-100.75 (%) which reflects good uniformity in drug content. All the formulations showed values within the prescribed limits for tests.

All the tablets were formulated using sodium bicarbonate as effervescent agent. It was observed that the carbon dioxide in presence of dissolution medium (0.1 N HCl) was trapped in the polymer decreases the density and by producing effervescence, the tablet will float in the media. The time required to float the tablet is known as floating lag time (FLT) and it was in the range of 38-42 sec. The total floating time (TFT) of the tablet was found to be >18 hrs. The results shown that the formulation have the good FLT and TFT which was shown in the Table 03.

*In vitro* dissolution studies of all the floating tablets were carried out in 0.1 N HCl. The study was performed for 6 hours and percentage drug release was calculated. All the formulations remained floating and intact through out the dissolution studies. The dissolution profile for the formulations is depicted in the Table-04 and Fig.02. The average of the three formulations was taken and at 6 hours the % drug release was found to be 11.55% respectively.

**Studies on Telmisartan floating tablets formulated with HPMC E50:**

Floating tablets of Telmisartan was prepared by using HPMC grade E50.Three batches were formulated using same concentration of HPMC and other ingredients. The Composition of the formulation was shown in Table-01. The floating tablets were formulated using fenugreek seed mucilage by wet granulation method.

The floating tablets are further evaluated for post-compression parameters like hardness, friability, weight variation, drug content uniformity, floating lag time and total floating time shown in the Table-03. The hardness of all the formulations ranges between 4.2-4.5 (kg/cm$^2$). All the tablets passed the weight variation test as the % weight variation was within the pharmacopeia limits of ±5. The tablets satisfied friability requirement, as the % friability values were less than 1%. The drug content estimations showed values ranges between 99.51-100.21 (%) which reflects good uniformity in drug content. All the formulations showed values within the prescribed limits for tests.

All the tablets were formulated using sodium bicarbonate as effervescent agent. It was observed that the carbon dioxide in presence of dissolution medium (0.1 N HCl) was trapped in the polymer decreases the density and by producing effervescence, the tablet will float in the media. The time required to float the tablet is known as floating lag time (FLT) and it was in the range of 29-33 sec. The total floating time (TFT) of the tablet was found to be >18 hrs. The results shown that the formulation have the good FLT and TFT which was shown in the Table-03.

*In vitro* dissolution studies of all the floating tablets were carried out in 0.1 N HCl. The study was performed for 6 hrs and percentage drug release was calculated. All the formulations remained floating and intact through out the dissolution studies. The dissolution profile for the formulations is depicted in the Table-23 and Fig.35. The average of the three formulations was taken and at 6 hrs the % drug release was found to be 10.03% respectively.

**Studies on Telmisartan floating tablets formulated with combination of HPMC K15 and E50:**

Floating tablets of Telmisartan was prepared by taking equal quantity HPMC grade K15 and E50 which finally gives the required amount of polymer (350 mg). Three batches were formulated using same concentration of HPMC and other ingredients. The Composition of the formulation was shown in Table-3.

**Comparison between the marketed conventional dosage form with our best released formulation i.e., HPMC K15:**

*In vitro* dissolution studies of optimized formulation and the marketed conventional dosage form (TELMI-40) were carried out in 0.1 N HCl. The conventional dosage form has the only the 9.94 % drug release at 6 hours as it has only the 39.7% bioavailability due to its less solubility and higher rate of elimination. The Telmisartan floating tablet formulated with HPMC K15 has the 11.55% drug release at 6 hrs. The rate of drug release was increased as it can present in the gastric region compared to conventional dosage form by increasing the solubility and decreasing the rate of elimination there by enhancing the drug release into the systemic circulation.

## CONCLUSION:

The present research work on formulation of Telmisartan as floating tablet by wet granulation technique improves its solubility and bioavailability by extending the gastric residence time. The floating tablets formulated with the HPMC K15 have shown the better amount of drug release when compared with the marketed conventional dosage form. Further investigation is required to evaluate the floating tablets of Telmisartan.

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