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# Formulation and *in-vitro* Evaluation of Eprosartan Floating Tablets.

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**Abstract:**

The Eprosartan is a selective ACE-II blocking agent which is used in the treatment of hypertension. In this study Eprosartan Floating tablets were prepared by using different polymers like HPMCK4M, HPMCK15M, HPMCK100M and CARBOPOL and HPC. Fifteen formulations of floating tablets of Eprosartan were developed by direct compression technique. The F9 formulation was found to be best of all the trials. The best formulation F9 can successfully be employed as a controlled release floating drug delivery system. The floating tablets can control the fluctuations in the plasma drug concentration, increase the gastric residence time and eventually improve the bioavailability of the drug. The FTIR study ruled out the drug-polymer interaction.

**Keywords:** *Eprosartan, Floating tablets, Controlled release, Floating drug delivery system.*

## Introduction:

Floating drug delivery system is also called the hydro-dynamically balanced system (HBS). Floating drug delivery systems (FDDS) have a bulk density less than gastric fluids and so remain buoyant in the stomach without affecting gastric emptying rate for a prolonged period of time. While the system is floating on the gastric contents, the drug is released slowly at the desired rate from the system. After release of drug, the residual system is emptied from the stomach. This results in an increased GRT and a better control of the fluctuations in plasma drug concentration. This delivery system is further divided into effervescent and non effervescent system (gas-generating system) [1-3].

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## (A) Non-effervescent systems:

**i. Colloidal gel barrier systems:**

Hydro-dynamically balanced system (HBS), which contains drugs with gel forming hydrocolloids, was first designed by Sheth and Tossounian in 1975. These systems incorporate a high level (20- 75%w/w) of one or more gel forming; highly swellable, cellulose type hydrocolloids, polysaccharides and matrix forming polymers. On coming in contact with gastric fluid, the hydrocolloids in the system hydrate and form a colloidal gel barrier around its surface. This gel barrier controls the rate of fluid penetration into the device and consequent release of the drug [4-6].

**ii. Micro-porous compartment systems**:

This technology is based on the encapsulation of a drug reservoir inside a micro porous compartment with apertures along its top and bottom walls. The peripheral walls of the drug reservoir compartment are completely sealed to prevent any direct contact of the gastric mucosal surface with the undissolved drug [7-9].

**iii. Multi-particulate system (Floating Beads)**:

Multi-particulate drug delivery systems are mainly oral dosage forms consisting of a multiplicity of small discrete units, each exhibiting some desired characteristics. In these systems, the dosage of the drug substances is divided on a plurality of subunit, typically consisting of thousands of spherical particles with diameter of 0.05-2.00mm. Thus multi particulate dosage forms are pharmaceutical formulations in which the active substance is present as a number of small independent subunits. To deliver the recommended total dose, these subunits are filled into a sachet [10-12].

**iv. Micro balloons:**

There are various approaches in delivering substances to the target site in a controlled release fashion. One such approach is using polymeric micro balloons as carrier for drugs. Hollow microspheres are known as the micro balloons. Micro balloons were floatable in vitro for 12 hrs, when immersed in aqueous media. Radio graphical studies proved that micro balloons orally administered to human were dispersed in the upper part of stomach and retained there for three hours against peristaltic movements [13-15].

## (B) Effervescent systems:

A drug delivery system can be made to float in the stomach by incorporating a floating chamber, which may be filled with vacuum, air or inert gas [16-18].

**i. Volatile liquid containing systems:**

These have an inflatable chamber which contains a liquid e.g. ether, cyclopentane, that gasifies at body temperature to cause the inflation of the chamber in the stomach. These systems are osmotically controlled floating systems containing a hollow deformable unit. There are two chambers in the system, first contains the drug and the second chamber contains the volatile liquid [16].

**ii. Gas generating systems**:

These buoyant delivery systems utilizes effervescent reaction between carbonate/bicarbonate salts and citric/tartaric acid to liberate $CO_2$ , which gets entrapped in the jellified hydrocolloid layer of the system, thus decreasing its specific gravity and making it float over time. A multiple unit type of floating pills, which generate $CO_2$, have also been developed. The system consists of a sustained release (SR) pill as seed, surrounded by double layers. The inner layer is an effervescent layer containing sodium bicarbonate and tartaric acid.

The outer layer is of a swellable membrane layer containing PVA, shellac etc. Another effervescent system consisting of a collapsible spring, which control the release of drug from the polymer matrix, has also been developed. The common approach for preparing these systems involves resin beads loaded with bicarbonate and coated with ethyl cellulose. The coating which is insoluble but permeable, allows permeation of water. Thus, carbon-dioxide is released, causing the beads to float in the stomach [17].

**Advantages of FDDS:**

Floating dosage systems form important technological drug delivery systems with gastric retentive behavior and offer several advantages in drug delivery [18]. These advantages include:

1. Improved drug absorption, because of increased GRT and more time spent by the dosage form at its absorption site.
2. Controlled delivery of drugs.
3. Delivery of drugs for local action in the stomach.
4. Minimizing the mucosal irritation due to drugs, by drug releasing slowly at controlled rate.
5. Treatment of gastrointestinal disorders such as gastro-esophageal reflux.
6. Simple and conventional equipment for manufacture.
7. Ease of administration and better patient compliance.
8. Site-specific drug delivery.

## Materials and Methods:

### Drug and Chemicals:

The drug used for the study was Eprosartan. All the chemicals/solvents like hydroxypropylmethylcellulose, mannitol, hydroxypropylcellulose, carbopol, sodium bicarbonate, talc *etc.* were of analytical/laboratory grade and obtained commercially.

## Results:

The composition of master formulation is depicted in **Table 1.**

**Table-1- Master Formulation**

| Ingredients (mg) | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 | F10 | F11 | F12 | F13 | F14 | F15 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Eposartan | 40 | 40 | 40 | 40 | 40 | 40 | 40 | 40 | 40 | 40 | 40 | 40 | 40 | 40 | 40 |
| HPMC K4M | 20 | 30 | 40 | - | - | - | - | - | - | - | - | - | - | - | - |
| HPMC K100 | - | - | - | 20 | 30 | 40 | - | - | - | - | - | - | - | - | - |
| HPMC K15m | - | - | - | - | - | - | 20 | 30 | 40 | - | - | - | - | - | - |
| HPC | - | - | - | - | - | - | - | - | - | 20 | 30 | 40 | - | - | - |
| Carbopol | - | - | - | - | - | - | - | - | - | - | - | - | 20 | 30 | 40 |
| Mannitol | 113 | 103 | 93 | 113 | 103 | 93 | 113 | 103 | 93 | 113 | 103 | 93 | 113 | 103 | 93 |
| $NaHCO_3$ | 15 | 15 | 15 | 15 | 15 | 15 | 15 | 15 | 15 | 15 | 15 | 15 | 15 | 15 | 15 |

| | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| MS | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 |
| Talc | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 |
| Wt. of Tablet | 200 | 200 | 200 | 200 | 200 | 200 | 200 | 200 | 200 | 200 | 200 | 200 | 200 | 200 | 200 |

**Floating time:**

The floating time of different formulations is given in **Table 2**.

**Table-2-Floating time of Different Formulations**

| Formulation | L.F.T (sec) {buoyancy time} | T.F.T (hrs) |
|---|---|---|
| F1 | 65 | 8 |
| F2 | 72 | 12 |
| F3 | 83 | 16 |
| F4 | 69 | 5 |
| F5 | 82 | 11 |
| F6 | 93 | 12 |
| F7 | 75 | 10 |
| F8 | 89 | 12 |
| F9 | 102 | 18 |
| F10 | 64 | 10 |
| F11 | 76 | 11 |
| F12 | 99 | 14 |
| F13 | 96 | 12 |
| F14 | 124 | 16 |
| F15 | 154 | 20 |

The spectral data (FTIR) of drug along with different polymers is depited in **Figure 1-5**.

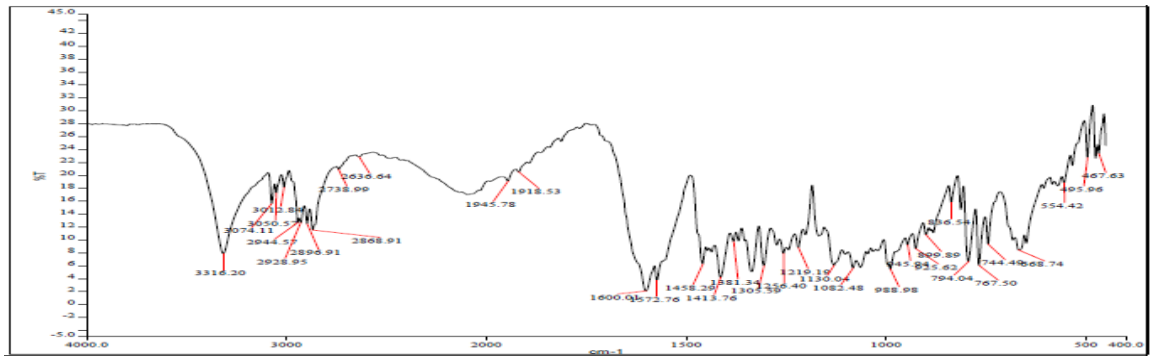


**Figure 1: FTIR Spectra of Eprosartan**

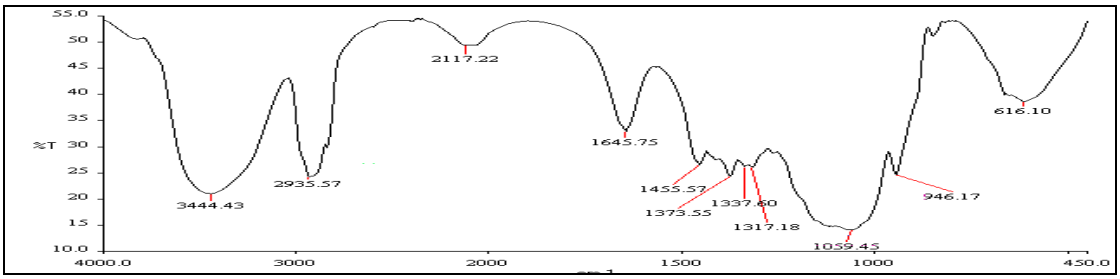


**Figure 2: FTIR Spectra of Eprosartan + HPMC**

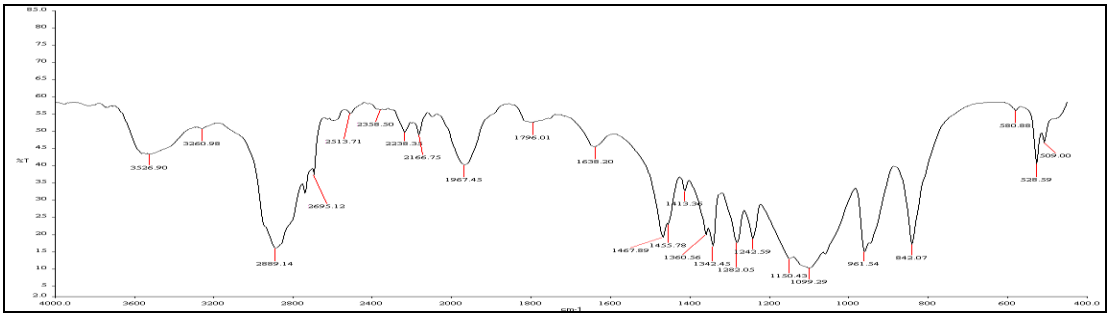


**Figure 3: FTIR Spectra of Eprosartan+ Carbopol**

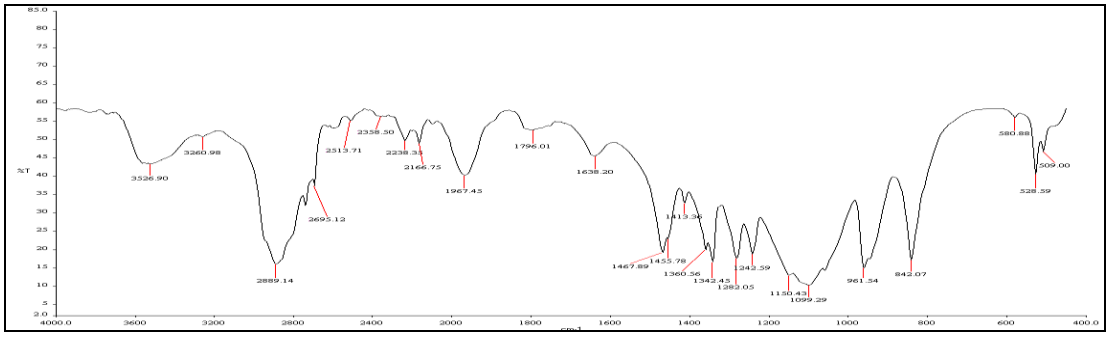


**Figure 4: FTIR Spectra of Eprosartan+ HPC**

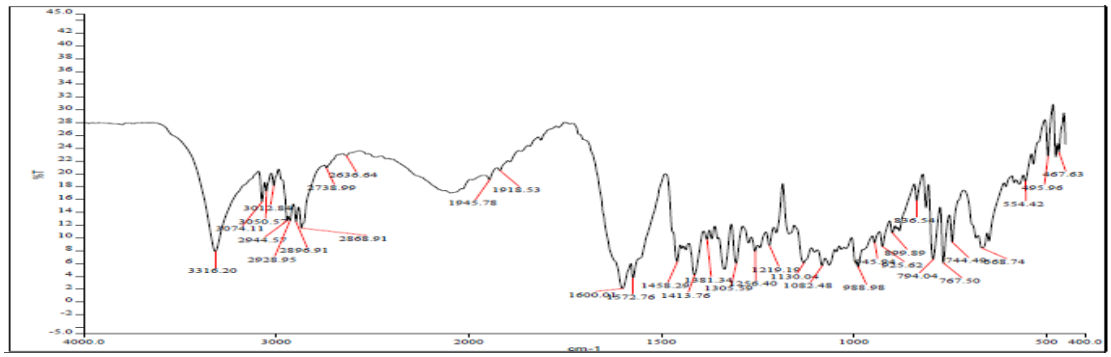

**Figure 5: FTIR Spectra of Optimized formula**

**Standard curve of Eprosartan:**

The Standard curve of Eprosartan is shown in **Figure 6.**

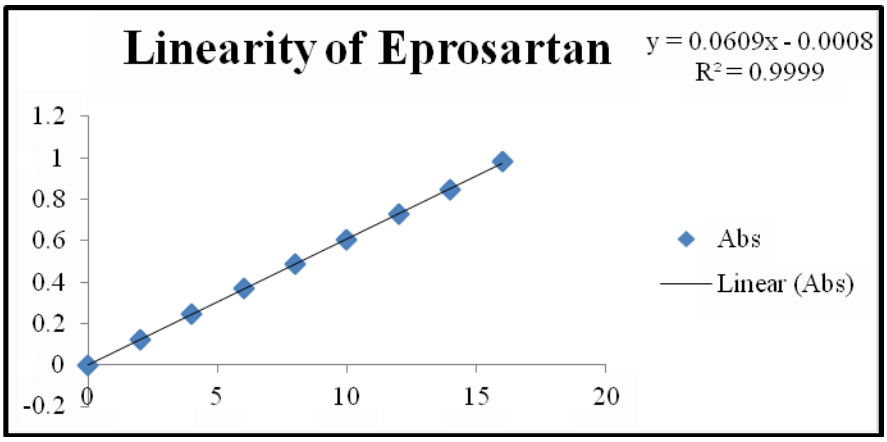


**Figure 6: Standard curve of Eprosartan**

**Flow Properties:**

The Flow properties of all prepared formulations (F1-F15) are given in **Table 4.**

**Table-4- Flow properties of all formulations F1-F15**

| Formulation | Angle of Repose (°) θ= $\tan^{-1}$ (h/r) | Loose bulk Density (LBD) (g/ml) | Tapped bulk Density (TBD) (g/ml) | Carr's index % | Hauser's ratio |
|---|---|---|---|---|---|
| F1 | $21^0$04 | 0.304 | 0.351 | 13.41 | 1.15 |
| F2 | $21^0$09 | 0.317 | 0.367 | 13.63 | 1.15 |
| F3 | $21^0$46 | 0.310 | 0.360 | 13.89 | 1.16 |

| | | | | | |
|---|---|---|---|---|---|
| F4 | $24^0$88 | 0.318 | 0.378 | 15.87 | 1.18 |
| F5 | $24^0$23 | 0.294 | 0.346 | 15.02 | 1.17 |
| F6 | $24^0$09 | 0.307 | 0.360 | 14.72 | 1.17 |
| F7 | $24^0$78 | 0.311 | 0.368 | 15.21 | 1.18 |
| F8 | $24^0$56 | 0.265 | 0.312 | 15.06 | 1.17 |
| F9 | $23^0$98 | 0.332 | 0.391 | 14.91 | 1.17 |
| F10 | $23^0$02 | 0.328 | 0.386 | 15.02 | 1.17 |
| F11 | $24^0$05 | 0.330 | 0.376 | 12.23 | 1.13 |
| F12 | $24^0$24 | 0.335 | 0.382 | 12.30 | 1.14 |
| F13 | $23^0$08 | 0.325 | 0.388 | 16.23 | 1.19 |
| F14 | $23^0$12 | 0.331 | 0.386 | 14.24 | 1.16 |
| F15 | $24^0$14 | 0.328 | 0.380 | 13.68 | 1.15 |

**Dissolution studies**

Dissolution profile of all formulations (F1-F15) is depicted in **Table 5** and **Figure 7**.

**Table-5-Dissolution studies of all Formulations F1-F15**

| | **1hr** | **2hr** | **4hr** | **6hr** | **8hr** | **10hr** | **12hr** | **14hr** | **16hr** |
|---|---|---|---|---|---|---|---|---|---|
| **F1** | 27.23 | 41.9 | 66.12 | 91.86 | 96.18 | -- | -- | -- | -- |
| **F2** | 22.54 | 35.12 | 50.34 | 63.87 | 77.02 | 96.56 | -- | -- | - |
| **F3** | 18.03 | 27.8 | 37.76 | 51.47 | 64.43 | 78.9 | 91.86 | 96.74 | -- |
| **F4** | 37.42 | 61.94 | 94.77 | -- | -- | -- | -- | -- | -- |
| **F5** | 24.44 | 35.82 | 49.44 | 70.89 | 85.82 | 95.34 | -- | -- | -- |
| **F6** | 19.6 | 32.46 | 50.56 | 65.67 | 78.36 | 89.55 | 96.26 | --- | -- |
| **F7** | 34.32 | 55.22 | 75.74 | 89.18 | 97.01 | -- | -- | -- | -- |
| **F8** | 28.73 | 45.9 | 61.94 | 73.5 | 85.07 | 95.9 | -- | -- | -- |
| **F9** | 17.16 | 26.86 | 36.94 | 48.88 | 60.44 | 69.4 | 78.54 | 87.31 | 98.5 |
| **F10** | 23.88 | 32.46 | 47.76 | 72.57 | 95.52 | -- | -- | -- | -- |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **F11** | 21.26 | 28.73 | 43.65 | 61.56 | 87.31 | 97.2 | -- | -- | -- |
| **F12** | 16.23 | 24.99 | 33.76 | 51.11 | 66.23 | 87.87 | 98.13 | -- | -- |
| **F13** | 25.37 | 41.6 | 55.59 | 80.41 | 94.02 | 97.76 | -- | -- | -- |
| **F14** | 28.73 | 32.46 | 46.08 | 56.15 | 71.26 | 80.22 | 91.6 | 96.82 | -- |
| **F15** | 17.72 | 26.86 | 36.19 | 43.47 | 57.64 | 69.77 | 78.54 | 90.67 | 97.94 |

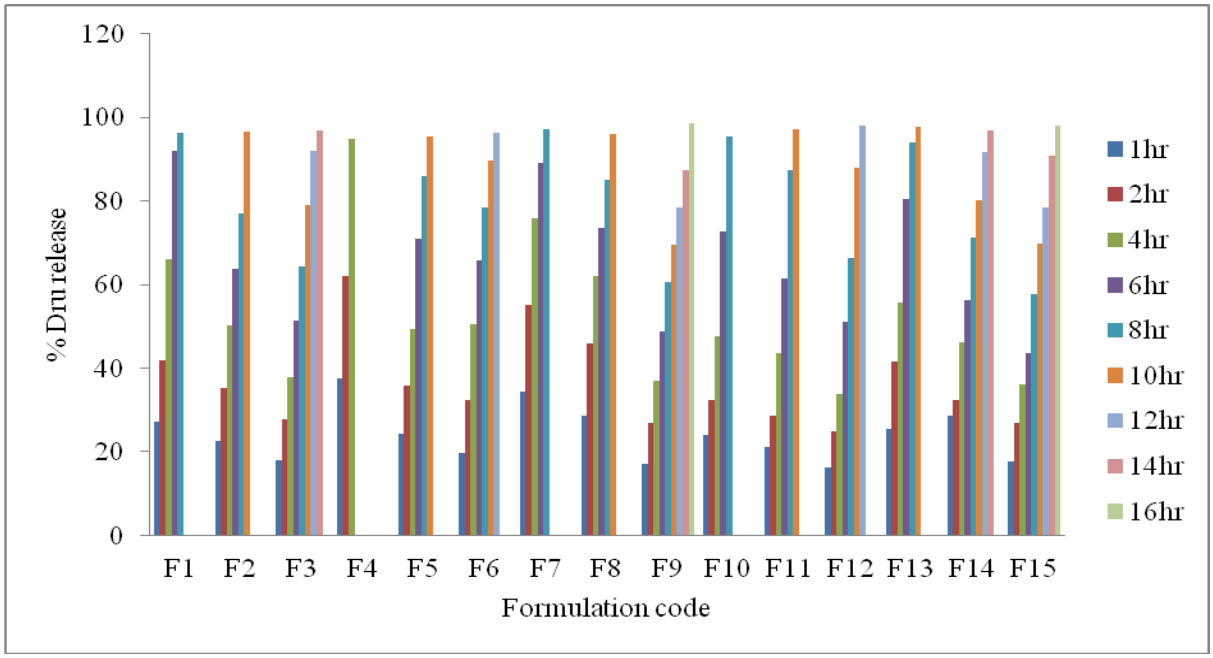


**Figure 7: Dissolution profile of all formulations F1 to F15**

**Evaluation:**

The various evaluation parameters of the prepared formulations (F1-F15) is given in **Table 6.**

**Table-6-Evaluation parameters of All Formulations F1-F15**

| Formulation | Uniformity of Weight mg | Hardness Kg/cm² | Diameter (mm) | Friability (%) | Drug content (%) |
|---|---|---|---|---|---|
| F1 | 201 | 5.1 | 8.7 | 0.435 | 98.70 |
| F2 | 200 | 5.4 | 8.7 | 0.492 | 99.25 |
| F3 | 199 | 5.3 | 8.7 | 0.501 | 99.42 |
| F4 | 200 | 5.5 | 8.7 | 0.463 | 98.52 |
| F5 | 201 | 5 | 8.7 | 0.478 | 98.24 |

| | | | | | |
|---|---|---|---|---|---|
| F6 | 202 | 5.2 | 8.7 | 0.342 | 98.63 |
| F7 | 198 | 5.5 | 8.7 | 0.414 | 98.15 |
| F8 | 200 | 5.5 | 8.7 | 0.417 | 99.42 |
| F9 | 200 | 5.2 | 8.7 | 0.318 | 99.14 |
| F10 | 198 | 5.1 | 8.7 | 0.412 | 98.46 |
| F11 | 199 | 5.2 | 8.7 | 0.416 | 98.10 |
| F12 | 204 | 5.2 | 8.7 | 0.514 | 98.65 |
| F13 | 201 | 5.1 | 8.7 | 0.355 | 98.32 |
| F14 | 198 | 5.3 | 8.7 | 0.411 | 98.65 |
| F15 | 202 | 5.1 | 8.7 | 0.441 | 98.02 |

## Summary and Conclusion:

The Eprosartan is a selective ACE-II blocking agent which is used in the treatment of hypertension. In this study Eprosartan tablets were prepared by using different polymers like HPMCK4M, HPMCK15M, HPMCK100M and CARBOPOL and HPC. Fifteen formulations of floating tablets of Eprosartan were developed by direct compression technique. The F9 formulation was found to be best of all the trials. The best formulation F9 can successfully be employed as a controlled release floating drug delivery system. The floating tablets can control the fluctuations in the plasma drug concentration, increase the gastric residence time and eventually improve the bioavailability of the drug. The FTIR study ruled out the drug-polymer interaction.

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