Research Article Chauhan et al., 8(7&8): July-Aug, 2017:5552-5558]
CODEN (USA): IJPLCP ISSN: 0976-7126

INTERNATIONAL JOURNAL OF PHARMACY & LIFE SCIENCES
(Int. J. of Pharm. Life Sci.)

Formulation development and evaluation of Gastroretentive floating tablet of Captopril using natural and synthetic polymer

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Abstract

The oral route of drug administration is the most important method of administering drugs for systemic effects. The parenteral route is not routinely used for self-administration of medication. The concept of floating drug delivery systems (FDDS) was first described in the literature as early as 1968, when Davis disclosed a method for overcoming the difficulty experienced by some persons of gagging or chocking while swallowing medical pills.

Keywords: Administration, gastroretentive, Floating Tablet

Introduction

An ideal dosage regimen in the drug therapy of any disease is the one which immediately attain the desired therapeutic concentration of drug in plasma and maintains it's constant for the entire duration of treatment. This is possible through the administration of conventional dosage forms in a particular dose and at particular frequency. The frequency of administration or dose interval of any drugs depends upon its half-life or mean residence time and its therapeutic index. In most cases, dosing interval is much shorter than the half-life of the drug, resulting in number of limitations associated with such a conventional dosage form which are, Poor patient compliance; increased chances of missing the dose of a drug with short half-life for which frequent administration is necessary

The topical route of administration has only recently been employed to deliver drugs to the body for systemic effects. It is probable that at least 90 % of all drugs used to produce systemic effects are administered by the oral route. When a new drug is discovered, one of the first questions a pharmaceutical company asks is whether or not the drug can be effectively administered for its intended effect by the oral route. If it cannot, the drug is primarily relegated to administration in a hospital setting or physician's office.

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Of drugs that are administered orally, solid oral dosage forms represent the preferred class of product. The reasons for this preference are well known.

Material and Methods

Captopril and Hpmc and All the reagents and solvents used were of analytical grade *In vitro* analysis of the prepared tablets was carried out as per the requirements of floating tablets as specified in official pharmacopoeia

Preformulation involves the application of biopharmaceutical principles to the physicochemical parameters of drug substance are characterized with the goal of designing optimum drug delivery system.

Physical Evaluation

The drug was taken in petriplate and its appearance was observed by naked eyes**.** The observation were recorded in table

Table 1: Physical Characters of Captopril

S. No	Name of Drug	Properties	Observation
1	Captopril	Colour	white
2		Odour	Odourless
3		Taste	Bitter
4		Texture	Amorphous

Table 2: Formulation of tablet using synthetic polymers

Sr. No.	Formulation code	Captopril (mg)	HPMC K15M (mg)	Na_2CO_3 (mg)	Carbopol (mg)	Lactose (mg)	Magnesium sterate (mg)	Citric acid (mg)	Total wt. (mg)
1	F1	50	40	30	20	30	20	10	200mg
2	F2	50	40	30	30	20	20	10	200mg
3	F3	50	32	30	25	33	20	10	200mg
4	F4	50	33	30	28	29	20	10	200mg
5	F5	50	38	30	20	32	20	10	200mg

Table 3: Formulation of tablet using natural polymers

S.N	Formulation code	Captopril (mg)	chitosan (mg)	Na_2CO_3 (mg)	Zenthen gum (mg)	Lactose (mg)	Magnesium sterate (mg)	Citric acid (mg)	Total wt. (mg)
1	F1	50	40	30	20	30	20	10	200mg
2	F2	50	40	30	30	20	20	10	200mg
3	F3	50	34	30	25	31	20	10	200mg
4	F4	50	30	30	35	25	20	10	200mg
5	F5	50	37	30	29	24	20	10	200mg

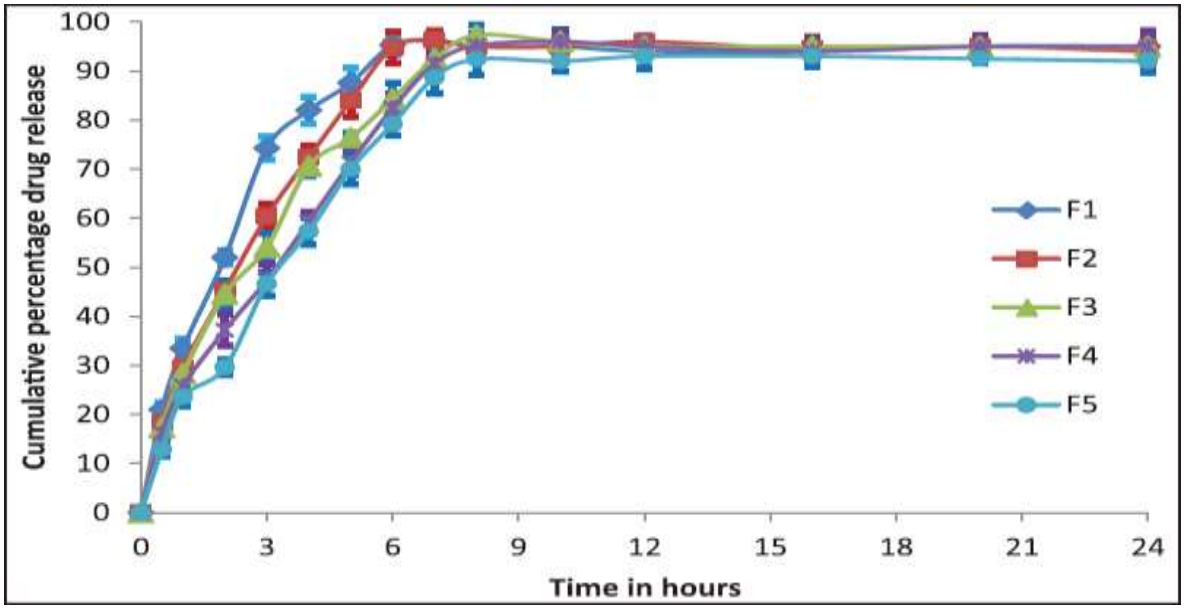
Table 4: Dissolution Profile of Captopril Floating tablet of using synthetic polymer

Time	Formulation				
(hr)	F1	F2	F3	F4	F5
1	19.21	20.45	18.35	17.96	15.35
2	25.36	22.38	24.55	20.89	19.88
3	34.25	31.85	35.36	39.25	31.58
4	49.21	45.29	47.25	40.96	42.66
5	61.45	59.03	62.38	65.34	56.69

6	72.22	76.25	78.29	81.02	76.25
8	79.65	76.25	78.65	81.02	71.04
10	83.03	80.96	84.36	89.25.	88.66

Table 4: Dissolution Profile of Captopril Floating tablet using natural polymer

Time	Formulation				
(hr)	F1	F2	F3	F4	F5
1	15.05	17.41	16.14	15.51	10.15
2	21.05	20.12	19.17	18.12	15.25
3	31.27	29.14	32.21	34.21	25.32
4	44.25	42.15	43.11	41.21	32.12
5	55.15	51.51	54.59	59.11	51.36
6	71.21	75.22	69.25	76.22	55.12
8	81.23	72.58	60.12	82.23	78.32
10	79.25	81.32	78.96	83.56	80.32



Graph 1: Dissolution curve of Captropril Floating tablet

The time taken for tablet to emerge on surface of medium is called the floating lag time (FLT) and duration of time the dosage form to constantly remain on surface of medium is called the total floating time (TFT). The buoyancy of the tablets was studied in USP 24 type II dissolution apparatus at 37±0.5 °C in 900 ml of simulated gastric fluid at pH 1.2.

As dictated by *in-vitro* dissolution data, the increase in the polymer concentration of HPMC K15M and progressively retarded the drug Table 9 and Figure 6. The lowest hpmc polymer concentration (F-4) showed faster release 88.66% in 10 hrs and the highest polymer concentration (F-1) released 83% drug after 10 hrs. When the concentration of the hydrophilic polymer was increased, the time taken for its swelling and erosion in the media was increased due to high viscous gel strength. The pore distribution became less on the effective surface area of the tablet which is exposed to the dissolution media. Therefore, the diffusion of the water insoluble drug from the matrix was retarded to its maximum and the drug release was slowed down. In the dissolution study it was observed that all the formulation having sustained release action.

Results & Discussion

Preformulation study

The physical characteristic of captopril powder was observed on different parameters viz. color, odour, taste and texture. The color, odour, taste and texture were found to be white, odorless, bitter and Amorphous in nature.

The Solubility of pure drug captopril was found very soluble in water and methanol, freely soluble in 0.1N HCl and soluble in 0.1N NaOH

The melting point was determined using melting point apparatus. The melting point of captopril was found to be 103˚C.

Captopril solution was scanned in the U.V. range of 200-400 nm using Systronic UV Visible spectrophotometer. The spectrophotometric method of analysis of captopril at λ_{max} 208 nm. The slope and intercept of the calibration curve were 0.016 and 0.006 respectively. The correlation coefficient 'r^2' values were calculated as 0.998.

Partition Co-efficient of captopril was determined in n-octanol: water (pH 7.4) and results of Partition co-efficient showed that the partition coefficient of captopril was found to be 0.960.

The FTIR spectra of drug with exipients were compared with the FTIR spectrum of the pure drug. It indicates no interaction between captopril and exipients.

Flow Properties of Powder Blend of Different batches of captopril

The powder blends of all the batches (F1-f5) of using synthetic polymer were evaluated on different parameters i.e. bulk density, tapped density and angle of repose (θ), Carr Index and Hausner's ratio. Bulk density of all batches (F1-F5) was found to be 0.40-0.51, 0.49-0.62, and respectively.

Tapped density all batches (F1-F6) was found to be 0.659, 0.660, 0.630, 0.672, 0.659 and 0.665 respectively.

Angle of repose was found to be 26.2;21.29,31.05,24.55,29.38 and respectively. Carr Index was found to be15.57,11.54,17.53,8.21,16.12and respectively. Hausner's ratio was found to be1.05,1.14,1.24,1.10,1.22respectively.

The values for angle of repose (<30) indicated Excellent flow properties of powder blends and index values and this was further supported by lower compressibility index values. Generally, compressibility index values less than 16 % result in good to excellent flow properties. The results shows that the all the powder blends have the good flow properties and compressibility which are essential for the preparation of the tablets from the powder blend.

Physical parameter for the formulations prepared by floating technique of using natural polymers is shown. Bulk density was found to be between 0.45 to 0.59g/ml and tapped desity between 0.52 .to 0.65g/ml, Hausner ration between 1.15 to 1.253. and angle of repose was found to be between 25.03 to 32.88, indicating fair to good flow properties. After determining these flow properties tablet was prepared.

Evaluation of Prepared Tablet of Different Batches of captopril

All the tablet formulations of different batches were evaluated for different evaluation parameters by using synthetic polymer viz. weight variation, hardness and friability thickness, total floating time. Weight variation of different batches (F1-F5) was found to be respectively. Weight variation with in limit so, it was concluded that the uniformity of drug distribution in the granulation or powder blend occurs. So, the tablets were made perfect.

In all formulation, the hardness test indicated good mechanical strength. Hardness of synthetic polymer was ranged from 5.4 to 6.0 Kg/cm^2. Friability was ranged from0.10 to 0.14..and weight variation range was 203 to 209 and content was ranged 96.99 to 99.09 total floating time>9 to>10 [hrs]

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In all formulation, the hardness test indicated good mechanical strength. Hardness of synthetic polymer was ranged from 5.2 to 5.9 Kg/cm^2. Friability was ranged from0.10 to 0.15..and weight variation range was 202 to 209 and content was ranged 92.99 to 97.09 total floating time>9 to>11 [hrs]

An ultraviolet (UV) spectrophotometric method was used for the determination of drug content. Absorption maxima were determined by scanning different concentration of solution of drug captopril An absorption maximum was 208nm nm and method obeys Beer's law in concentration range 10 to 5. µg/ml, with good correlation coefficient (0.998).

In weight variation test, 20 tablets were selected random and average weight variation was calculated. Then individual tablet were weighed and weight was compared with average weight. It was varied from 203 to 209.10.

***In-vitro* release of captopril**

In vitro release the release study in vitro aqueous Floating tablet of captopril time period 12 hours.

In the disintegration test, the disintegration test of different formulation it was observed that disintegration time of captopril ranged from 23 to 28 min. in 0.1N HCl.

The release profile of captopril from the timed – Floating tablet of different batches had been studied . *In vitro* dissolution studies was carried out USP paddle metod at 50rpm in 900ml of 0.1NHCL, maintained at 37+0.5^{0}C.10 ml of aliquots withdrawn atb specified intervals filtered through whatmann filter paper and analysed at 208 nm using UV-VCisible spectrophotometer. The dissolution media was replaced by 10ml of each fresh dissolution fluid to maintain a constant volume. The synthetic polymer lower concentration (f-4) showed faster release89.25% in 10 hrs and the highest polymer concentration (f-2} released 80% drug after10 hrs same as synthetic polymer comparatively the release rate of using natural polymer f4 lower polymer concentration and shows fasterr releas83.23 % and higher polymer concentration f1 shows slower release after 10 hrs 79.25

The work carried out to study the effect of other response like bioadhesiveness and floating , release rate of drug. Formulation which are using synthetic polymers turned out to be the best because they showed a minimum lag time and maximam floating time with maximum release of drug persrntage so it is considerd as a successful

Hence in present investigation,for the formulation of floating tablet hpmc and carbopol used as matrix forming agent.other excipient used are, sodiumbicarbonate{as a gas generating agent} citric acid magnesium stearate as lubricant. The drug polymers are subjected to various preformulation stidies sach as angle of repose, bulk dencity,tapped dencity, compressibility index,hausner ratio cherecterization using FTIR ,drug and excipient compatibility the tablet were using single station punching machine. Prepared tablet were subjected to various evaluation parameters such as thickness hardness,weighet variation, friability buoyancy study and invitro drug release, it was councluded that there was no interference in the functional group as the principle peaks of the drug were found to be unaltered in the drug polymer physical mixture Floating, bioadhesive, swellable and megnatic system based GRTB are available however floating is gaining popularity associated whith their negligible advers effect on motality of gi tract andachevment of immediate buoyancy for GRTB be successful,detailed understanding of physiochemical property of drug physiological events of drug in the gi tract impact of gi tract physiology On drug delivery and formulation stratergies and their evaluation is prerequieste

Conclusion

Floating tablets used for the drugs which get easily solubilized in stomach captopril floating tablets was used for the tratment of hypertension. The choice of the polymer and its quantity in floating tablet is critical to control the solubility profile of tablet. Drugs which are having low oral bioavailability (<50%), short biological half life (about 1 to 1.9 hrs.) and an adequate protein binding that are preferred while formulating floating tablet. On the basis of findings observed in present work, it can concluded that floating tablet of captoprilcould be the suitable dosage form for the treatment of diabetes with low dosing frequency for better patient compliance, less toxic & better hypertension than other floating tablet formulations. This dosage form is preferred as it is very convenient and easy to formulate, cost-effective and does not require high cost equipments. For that reason, this dosage form has been gaining so much

attention nowadays. From the above experimental result it can be concluded that, sodium bicarbonate has predominant effect on the buoyancy lag time, while hpmc has predominant effect on the total floating time and drug release.

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How to cite this article

Chauhan S., Tahilani P., Goyanar G. and Banweer J. (2017). Formulation development and evaluation of Gastroretentive floating tablet of Captopril using natural and synthetic polymer. *Int. J. Pharm. Life Sci.*, 8(7&8):5552-5558.

Source of Support: Nil; Conflict of Interest: None declared

Received: 15.04.17; Revised: 21.05.17; Accepted: 21.07.17