



FORMULATION AND EVALUATION OF ATENOLOL FLOATING TABLETS BY USING PEANUT HUSK POWDER AS A NATURAL POLYMER

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ABSTRACT

In the recent years, scientific and technological advancements have been made in the research and development of novel drug delivery systems by overcoming physiological troubles such as short gastric residence times and unpredictable gastric emptying times. Gastro retentive drug delivery systems are the systems which are retained in the stomach for a longer period of time and thereby improve the bioavailability of drugs. Floating drug delivery system is one of the several techniques currently used to formulate a successful gastro retentive drug delivery system. Floating drug delivery systems (FDDS) have a bulk density less than gastric fluids and so remain buoyant in the stomach without affecting the 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. In the present research we have studied pea nut husk powder as a floating agent. Floating tablets were prepared by direct compression method using Atenolol and in various concentrations of the polymers HPMC K100M and Peanut Husk powder. Among three formulations F1 has shown a drug release of 94.2% after 12hrs and F1 has shown a floating lag time of 1.07mins. Based on in vitro dissolution studies and floating studies, increased concentration of peanut husk powder improves the floating nature but drug release is retarded due to increase in concentration of HPMC K100M. The optimized formulation followed Higuchi kinetics. It can be concluded that peanut husk powder can be a promising low density material in the formulation of gastro retentive floating drug delivery systems in combination with synthetic polymer HPMC K100M.

KEYWORDS: Floating Drug Delivery System, Peanut Husk Powder, Atenolol, Natural Polymer

INTRODUCTION

Oral drug delivery is the most widely utilized route of administration among all the routes that have been explored for systemic delivery of drugs via pharmaceutical products of different dosage forms. It is uncomplicated, convenient and safe due to its ease of administration, patient acceptance and cost effective. Gastro retentive drug delivery systems are the system which are retained in stomach in longer period of time and thereby improve bioavailability of drug.¹⁻³ Several techniques are used to formulate a successful Gastro retentive drug delivery system such as floating drug delivery system, bio-adhesive system, high density system and magnetic system.⁴ The need for gastro retentive dosage forms (GRDFs) has led to extensive efforts in both academia and industry towards the development of such drug delivery systems. Prolonging the gastric residence of a dosage form may be of therapeutic value. Amongst the methods available to achieve this, floating dosage forms show considerable⁵. The basic idea behind the development of such a system is to maintain a constant level of drug in the blood plasma in spite of the fact that the drug does not undergo disintegration. The drug usually keeps floating in the gastric fluid and slowly dissolves at a predetermined rate to release the drug from the dosage form and maintain constant drug levels in the blood⁵.

Atenolol is a cardio selective β_1 -adrenergic receptor blocking agent without membrane stabilizing or intrinsic sympathomimetic activity and it has been used for hypertension. It is poorly absorbed from the lower gastrointestinal tract. The oral bioavailability of Atenolol has been reported to be 50%. The increase in GRT may increase the extend of absorption bioavailability of drug. The drug is slightly water soluble. It has elimination half-life 6-7hrs. The aim of this study was to develop effervescent gastro retentive floating tablet using Atenolol natural peanut husk powder as a light floating material along with synthetic polymer like HPMCK100M. The purpose of the study is to develop gastro retentive floating tablet of Atenolol which should remain in the stomach of upper part of GIT for prolonged period of time with the view to improve bioavailability of the drug as well as its half-life and to control the rate of release of the drug in physiological environment of stomach.

MATERIALS AND METHODS

Materials

Atenolol Was Obtained as gift sample from Yarrow Chem, Mumbai, Sodium Bicarbonate, Magnesium Stearate, Talc, Lactose, was obtained from Nice Chemicals Pvt. Ltd, India. Peanut Husk Powder was collected from seeds of Arachis hypogea in Erode. All other chemicals were of analytical grade.

Preparation of peanut husk ⁶

The seeds of peanuts were collected from the fields in erode district. These seeds were dried in an oven at 40 °c for 3 hours and the surface layer was removed from the seeds by crushing them with hand. The husk was milled into fine powder by using mixer grinder. The obtained peanut husk powder was passed through sieve number 100 and fine powder was stored in a desiccator for further use

Preparation of gastro retentive floating tablet of Atenolol ^{7,8}

Gastro retentive floating tablet of Atenolol was prepared by direct compression method using sodium bicarbonate as gas generating agent, HPMC K100M, peanut husk were used as rate controlling polymer. All the ingredients were weighed accurately and mixed homogeneously in the quantity mentioned in the table no: 1 .The drug and excipients were passed through sieve number 80 and mixed uniformly for 3 minutes. Then the powder blend was lubricated with the talc and magnesium stearate and compressed into tablet of 250 mg each using 10 punch rotatory tablet compression machine having the diameter of 8 mm flat faced punch.

TABLE NO 1: LIST OF INGREDIENTS USED IN THE FORMULATION

S.no	Ingredients	F1	F2	F3
1	Atenolol	25	25	25
2	HPMC K 100	138	163	175
3	Peanut husk	30	25	13
4	Sodium bicarbonate	20	20	20
5	Lactose	27	7	7
6	Magnesium stearate	5	5	5
7	Talc	5	5	5

Evaluation of powder blend (pre-compression parameter)

Compatibility studies ⁹

Compatibility studies were performed using IR spectrophotometer. The IR spectrum of pure drug and physical mixture of drug and polymer were studied. Drug- excipient interactions play a vital role with respect to release of drug from the formulation amongst others. FTIR techniques have been used here to study the physical and chemical interaction between drug and excipients used.

Angle of repose

In order to determine the flow property the angle of repose was performed by funnel method. The maximum angle can be obtained between the free standing surface of the powder heap and the horizontal plan. Accurately weighed powders are taken in a funnel and height of the funnel was adjusted in such a way the tip of funnel just touched the apex of the heap of powder (2.0 cm above hard surface) the powder were allowed to flow through the funnel freely onto the surface. The diameter of the powder concentration was measured and angle of repose was calculated using the following equation.

$$\tan \theta = h/r$$

θ = angle of repose
 h = height
 r = radius

Bulk density (Db) ² and Tapped density (Dt)

A quantity of 5g of the powder (W) from each formula was introduced into a 25 ml measuring cylinder. After the initial volume was observed, the cylinder was tapped on a hard surface. The tapping was continued until no further change in volume was noted. The bulk density and tapped density were calculated, using the following formula and they are expressed in gm/ml

$$\text{Bulk Density} = W / V_o$$

$$\text{Tapped Density} = W / V_f$$

Where W = Weight of the powder,

V_o = Initial Volume, V_f = Final volume.

Compressibility index and Hausner's ratio

Compressibility index is an important measure that can be obtained from bulk and tapped density. The less compressible material more flowable it is. If the material having values of less than 20-30 %, it is defined as free-flowing material.

$$\text{Compressibility index (CI)} = \{(Dt - Db) \times 100\} / Dt$$

Hausner ratio is the indirect index of measuring the powder flow and it is calculated by using the following formula

$$\text{Hausner's ratio} = \text{tapped density} / \text{bulk density}$$

Post Compression Parameters¹⁰

The formulated tablets were evaluated for Thickness, Hardness, Weight variation, Friability, Drug content, Uniformity of content, In-vitro Drug release, Buoyancy lag time (BLT), Total floating time (TFT).

Thickness

The thickness of the tablets was determined by using Vernier Calipers. Five tablets from each formulation were used and average values are calculated.

Weight variation

Twenty tablets were selected randomly from each batch, individually weighed in a single pan electronic balance and the average weight is calculated. The uniformity of weight is determined according to I.P. specification. As per IP specifications not more than two of individual weights should deviate from average weight by more than 5% deviate more than twice that percentage.

Hardness

Tablet requires certain amount of strength or hardness and resistance to withstand mechanical shocks of handling during manufacture, packing and shipping. Monsanto hardness tester is used to measure the hardness of tablet. Three tablets from each batch are used for hardness test and results are expressed in Kg/cm².

Friability

The friability of tablets was determined using Roche friabilator apparatus. Pre-weighed samples of 20 tablets are placed in the friabilator, which is then operated for 100 revolutions at 25 rpm. The tablets are then dusted and reweighed. The percentage friability is calculated by the following expression and less than 1% is considered acceptable.

$$\text{Friability} = \frac{W_0 - W_1}{W_0}$$

Drug content uniformity:

Ten tablets are weighed and taken in a mortar and crushed to make powder form. A quantity of powder weighing equivalent to 10mg of drug is taken in 100ml volumetric flask and 0.1M HCl was added. The solution is filtered using membrane filter (0.45µm) and 10 ml of filtrate is taken into 100 ml volumetric flask and made up to final volume with 0.1M HCl. Then its absorbance is measured at 225nm using UV-Visible spectrometer. The amount of drug present in one tablet is calculated using standard graph.

Swelling Index study

From each formulation, one tablet is weighed and placed in a USP type II paddle dissolution test apparatus containing 900ml of 0.1N HCl with the paddle speed of 50rpm. After predetermined time the tablet is removed from apparatus, blotted to remove excess of water and weighed on digital balance. The increase in the wet mass represents the medium uptake (swelling index). The percentage weight gain by the tablet is taken as swelling index & expressed in terms of percentage, and it is calculated from the following equation.

$$\text{SI (\%)} = \frac{W_t - W_0}{W_0} \times 100$$

Where, SI is swelling index, W_t is weight of tablet at time t, W₀ is weight of tablet before immersion.

In vitro buoyancy study ¹¹

The *in-vitro* buoyancy studies are performed for two parameters such as floating lag time (FLT) and total floating time (TFT). These parameters are determined for all the formulations of Atenolol. The randomly selected tablets from each formulation are kept in a 100ml beaker containing 0.1M HCl. The time taken for each tablet to rise on the surface and float is taken as floating lag time (FLT). The total floating time of all tablets are performed by using dissolution test apparatus USP type II paddle method with a stirring speed of 50 rpm at 37°C ± 0.5°C in 900 ml of 0.1M HCl for 12 hours. The duration of time the floating tablets constantly remain on surface of medium is taken as total floating time (TFT).

In vitro drug release studies ¹²

Dissolution characteristics of the formulated floating tablets of Atenolol are carried out using USP type II (paddle) dissolution test apparatus for 12hrs. The dissolution test was performed by using 900 ml of 0.1 N HCl in dissolution apparatus and temperature of the medium was set at 37°C ± 0.5°C. One tablet of different formulation is placed in each dissolution vessel and the rotational speed of paddle was set at 50rpm. 1ml of sample is withdrawn at predetermined time interval of every hour for up to 12 hours and same volume of fresh medium was replaced immediately. The withdrawn sample of 1ml was diluted to 10ml volumetric flask and further diluted three times by taking 1ml of the sample to 10ml and filtered and filtered through 0.45µ membrane filter. The resultant sample are analyzed for drug content at 225nm using UV-Visible spectrophotometer. The cumulative percentage drug release was determined from the absorbance and the graph was plotted against time (hrs).

In vitro release kinetics studies ¹³

The dissolution data are fitted to four popular release models such as a zero order, first order, Higuchi and Korsmeyer-Peppas's equations. The order of drug release from matrix systems is studied by using Higuchi equation and Erosion equation. For finding out the mechanism of drug release from gastro retentive floating tablets of Atenolol, the dissolution data obtained from the above experiments are treated with the different release kinetic models.

Zero order release equation: $Q = K_0t$

Higuchi's square root of time equation: $Q = K_H t^{1/2}$

Peppas's equation: $F = Mt/M = K t^n$

Release kinetics model had described drug dissolution from solid dosage form where the dissolved amount of drug is the function of drug release in order to study the exact mechanism of the drug release from the tablet drug release data was analysed according to

zero order, first order, Higuchi square root and korsmeyer-peppas model. The criteria for selecting the most appropriate model was chosen on the basis of goodness of fit test

Stability studies:

Stability testing was conducted at $40^{\circ}\text{C} \pm 2^{\circ}\text{C} / 75\% \text{ RH} \pm 5\% \text{ RH}$ for 3 months using stability chamber (Thermo Lab, Mumbai). Samples were withdrawn at predetermined intervals 0, 30, 90, and 180 days period according to ICH guidelines¹⁴. Various in vitro parameters such as drug content, in vitro release studies and floating lag time were evaluated.

RESULTS AND DISCUSSION

The compatible studies were performed by using IR spectrophotometer.

FTIR spectra's of pure Atenolol, polymer and blend of polymers with drug were determined. Drug excipients interaction plays an important role with respect to drug release from the formulation among the others FTIR technic have been used to study the physical and chemical interaction between the drug and excipients used. Atenolol showed that the principal IR peaks at 2924.85cm^{-1} , 3414.73cm^{-1} , 3441.74cm^{-1} , 1127.32cm^{-1} , 3555.91cm^{-1} , 1637.45cm^{-1} . All the major peaks present in the spectrum of pure drug of Atenolol and polymers HPMC K100M, Peanut Husk powder were clearly observed in the spectrum of physical mixtures and formulation with negligible changes, thus indicating the compatibility of the drug Atenolol and other ingredients in different formulation. The obtained results clearly showed that there was no interaction between the drug and polymers.

Precompression evaluation of the Atenolol Powder Blend

All the observations of Pre-compression parameters were within the prescribed limits of IP 2018. The various micrometric properties of the different formulation F1 to F3 were studied. Acceptable range of angle of repose is of 20 to 40 and the angle of repose for the prepared blend range was between 25.94 to 29.42, which indicate good flow property in acceptable range (Table No: 2). Hausner's ratio is up to 1.25; the Hausner's ratio for prepared powder blend was between 1.23 to 1.25 there by exhibiting good flow property. The acceptable range of Carr's index is of 5 to 21% thus Carr's index of the powder blend was found between 19.61 to 20.60 and hence had good flow property.

Table No: 2 Micrometric Properties of the Powder Blend

Formulation Code	Angle of Repose(θ)	Bulk Density(G/Cm^2)	Tapped Density(G/Cm^2)	Carr's Index (%)	Hausner's Ratio
F ₁	$25.94' \pm 0.24$	0.320 ± 0.36	0.402 ± 0.27	20.39 ± 0.15	1.25 ± 0.41
F ₂	$26.05 \pm ' 0.25$	0.323 ± 0.41	0.400 ± 0.25	19.25 ± 0.17	1.23 ± 0.43
F ₃	29.42 ± 0.30	0.332 ± 0.38	0.413 ± 0.27	19.61 ± 0.21	1.24 ± 0.42

EVALUATION OF GASTRO RETENTIVE FLOATING TABLETS OF ATENOLOL

All the formulations had average tablet weight in the range of 248.5 to 249.5mg. Thickness ranges between 3.8 and 4mm. The mean hardness for all formulation was between $3.0 \text{ Kg}/\text{cm}^2$ and $3.5 \text{ Kg}/\text{cm}^2$. The friability of all the gastro retentive floating tablets of Atenolol was found between 0.59 % and 0.61%. The drug content ranged between 99 % to 101 %. The thickness depends upon the size of the punch (8mm) and the weight of the tablet (250mg). Friability is needed for the tablets to withstand force of compression applied during the manufacture of tablets and all the formulated floating tablets of the Atenolol were shown the percentage friability within the official limits (not more than 1 %). formulation showed favorable drug content which were within the specifications Table No:3

Table No: 3 Post Compressional Evaluations of Gastro Retentive Floating Tablets of Atenolol

Formulation Code.	Thickness (mm)	Diameter (mm)	Hardness (Kg/Cm^2)	Friability (%)	Average Weight (mg)	Drug Content \pm SD
F ₁	4.1 ± 0.15	8 ± 0.1	3.0 ± 0.33	0.60 ± 0.50	249.5 ± 0.23	99.8 ± 1.05
F ₂	3.8 ± 0.28	8 ± 0.1	3.0 ± 0.24	0.61 ± 0.41	249.0 ± 0.25	99.3 ± 1.06
F ₃	3.8 ± 0.24	8 ± 0.2	3.5 ± 0.25	0.59 ± 0.36	248.5 ± 0.28	99.7 ± 1.02

Evaluation of floating properties¹⁵

The tablets were placed in 100ml beaker containing 0.1N HCl. The time required for the tablets to raise the surface and float was the floating lag time. The In vitro buoyancy properties of the gastric retentive floating tablets of Atenolol were showed in the table no: 4

Table No: 4 In Vitro Buoyancy Properties of the Gastric Retentive Floating Tablets of Atenolol

Formulation code	Floating lag time in mins	Total floating time in hrs	Swelling index (%)
F1	1.07 ± 0.21	>12	196
F2	1.08 ± 0.33	>12	192
F3	3.25 ± 0.25	>12	189

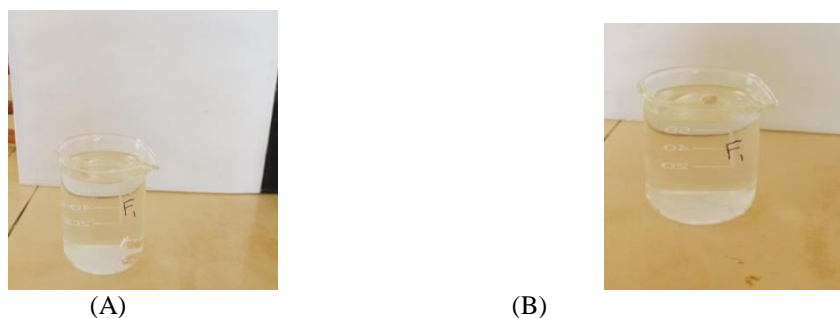


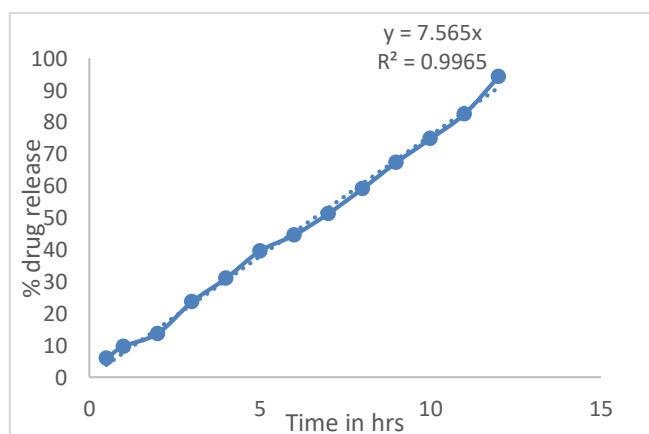
Figure 1 Floating Property of the Atenolol Tablet F1 (A) at initial time, (B) after 1.07 minutes

The gastro retentive floating tablets formulations of F1, F2 and F3 was made by using high viscosity polymer such as HPMC K100M and natural polymer of peanut husk powder. The floating tablet formulation of F1 comprises of high viscosity polymer of HPMC K 100M and natural polymer peanut husk powder in the ratio of 55:45 because of low concentration of HPMC K100M and high concentration of peanut husk powder when compared to other formulation it floats in 1.07 mints Fig 1. The floating tablet formulation of F2 comprises of high viscosity polymer of HPMC K 100M and natural polymer peanut husk powder in the ratio of 65:35 because of the more concentration of HPMC K100M and less concentration peanut husk powder is slightly increased when compared to F1. The formulation F3 comprises of high viscosity polymer HPMC K100M natural polymer peanut husk in the ratio of (70:30) due to high concentration of HPMC K100M and low concentration of peanut husk powder the floating lag time was increased when compared to F1. The gas generated cannot be entrapped inside the gelatinous layer and it escapes leading to in variation in floating lag time and total floating time

In vitro dissolution study^{16,17}

Floating formulation mainly affected by physiological condition such as food transport gastro intestinal motility and so on. A study on floating tablet of Atenolol as indicated lower bioavailability of drug reason for this lower bioavailability is due to small size of the dosage form, causing too short residence time different polymers and their combinations were used in the formulation of gastro retentive floating tablet of floating Atenolol it was observed that the percentage of polymer influences the drug release pattern. The percentage release profile was shown in the table it significantly high rate and extend of drug release was observed from the formulation F1 based on ratio of HPMC K100M and peanut husk powder. The combination of high percentage of HPMC K100M and the formulation provides drug release for longer time. The lower percentage of peanut husk present in formulation F3 the floating lag time was increased. The in vitro drug release study of Atenolol tablets was carried out in 0.1N HCl pH1.3 for 12hrs. The plot of time in hour's vs percentage cumulative drug release was plotted. In vitro drug release of the drug release was carried out for 12 hours and In vitro drug release studies of the formulations F1, F2, F3 containing HPMC K100M and peanut husk in the ratio of F1(55:45), F2 (65:35), F3(70:30) showed the drug release of 94.2%, 88.9% ,86.8 % respectively at the end of 12 hrs Fig 2. Among all the formulations F1 (HPMC K 100 55%, Peanut husk powder 45%) was optimized on the basis of invite drug release, floating lag time and total floating time. It showed maximum drug release in the controlled manner (94.2% in 12hrs).

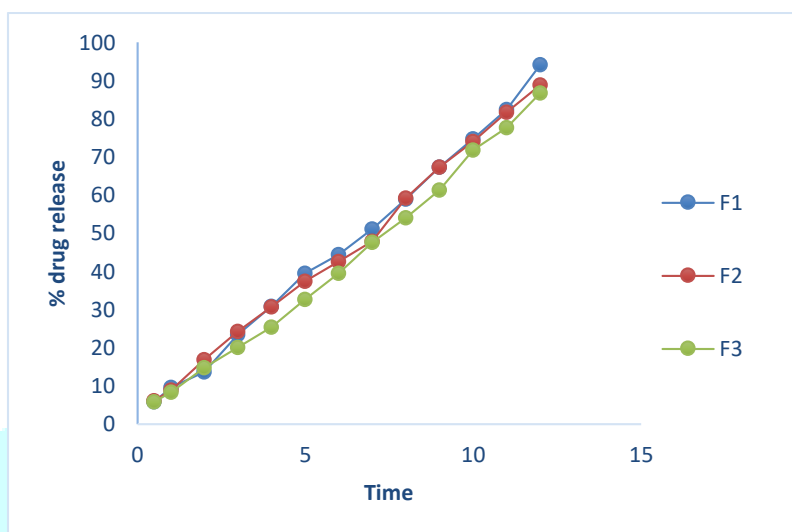
Figure: 2 Percentage of Drug release of the optimized formulation F1



Drug release kinetics studies¹⁸

The drug release kinetics of gastro retentive floating tablets of Atenolol was analyzed according to different kinetic equations such as by zero order, first order, Higuchi, and korsymeyer-peppas. The data were analyzed by the regression coefficient method and regression coefficients (R²) of all formulations are found. The formulations F1, F2, F3 followed zero order and korsymeyer-peppas model release kinetics Fig 3. The invitro release (R²=0.9985 to 0.9991) confirm the diffusion mechanism, the data was fitted into korsymeyer-peppas equation the formulation showed good linearity of R² = 0.9863 to 0.9937.

Figure no: 3. Release kinetics of zero order models for F1, F2 and F3

**STABILITY STUDIES**

There were no changes observed in percentage drug content, in vitro drug release studies and floating lag time during storage of the optimized formulation F1 for 6 months; hence, the optimized formulation F1 was found to be stable.

CONCLUSION

The gastro retentive floating drug delivery is a promising approach to achieve increase gastric retentive time and thereby improves its bioavailability with the addition of gel forming polymer HPMC K100M, Natural polymer peanut husk powder and gas generating agent sodium bicarbonate. These agents were essential to achieve invitro buoyancy with the ratio of 55: 45 of synthetic polymer HPMC K100M and natural polymer peanut husk powder which showed better control over the drug release. The formulated tablets (F1 to F3) showed acceptable weight variation, hardness and uniformity of drug content with lesser FLT and prolonged floating duration could be achieved by sodium bicarbonate and peanut husk powder exhibited and higher swelling index. Polymer swelling is crucial in determining the drug release rate and important for floatation. The release kinetics data was analyzed according to different kinetic equation by the regression coefficient method and regression coefficient value (R²) of all formulations F1 to F3 followed korsymeyer-peppas model and zero order kinetics. The objective of formulating gastro retentive floating dosage form of Atenolol the using optimized techniques has been achieved. It can be concluded that gastro retentive floating tablet of Atenolol can be formulated by using different ratio of HPMC K100M and peanut husk powder with good release profile for a prolonged period of time up to 12hrs which decreases the frequency of dose administration and improves patient compliance.

REFERENCE

- Chien YW. Novel Drug Delivery Systems. Informa health care USA, New York. 2011; 2nd ed: pp.164-69.
- Robinson JR, Lee VHL. Controlled Drug Delivery. Informa health care USA, New York.2011; 2nd ed: pp. 253-57.
- Jain NK. Controlled and Novel Drug Delivery. CBS Publishers & Distributors, New Delhi.2010;1st ed:pp. 5-7.
- Chandra Sekhara Rao G, Ramadevi K, Soujanya V,Prasad Ch.Formulation and Evaluation of Floating Matrix Tablets of Ramipril Using Peanut Husk Powder. International Journal of Pharmaceutical Development & Technology.2013; 3(2):72-79.
- Rao BP, Kottan NA, Sncith VS. Ramesh C. Development of Gastro retentive drug delivery system of cephalixin by using factorial design. ARS Pharmaceutical. 2009; 50(1):8-24.
- Peanut available from: [URL:http://en.wikipedia.org/wiki/peanut](http://en.wikipedia.org/wiki/peanut).
- Gambhire MN, Ambade KW, Kurmi SD, Kadam VJ, Jadhav KR. Development and invitro evaluation of an oral floating matrix tablet Formulation of Diltiazem hydrochloride.AAPS Pharm Sci Tech. 2007 Sep ; 8(3): E166-74. DOI: <https://doi.org/10.1208/pt0803073>
- Patel SS, Ray S, Thakur RS. Formulation and evaluation of floating drug delivery system containing Clarithromycin for Helicobacter pylori. Acta Pol Pharm.2006 Jan-Feb;63(1):53-61.
- M.Purushothaman,C.Saravanan.Formulation and Evaluation of Metaprolol Succinate Floating Tablets Using Peanut Husk Powder as Natural Polymer.International Journal of Chem Tech Research.2017;10(10):169-77.
- Jaimini M, Rana AC, Tanwar YS. Formulation and evaluation of Famotidine floating tablets. Curr Drug Deliv. 2007 Jan; 4(1):51-5. DOI: 10.2174/15672010779314730

11. Thahera PD, Ashok, Latha K, Shailaja T, Nyamathulla S, Uhumwangho MU. Formulation and evaluation of Norfloxacin gastroretentive drug delivery systems using natural polymers. International current pharmaceutical journal. 2012 Jun 03;1(7):155-64. DOI:<http://dx.doi.org/10.3329/icpj.v1i7.10809>
12. Swarna Kamala Chinthala CHI, Srinivas Reddy Kota K, Hadassah M, Hepsibha Metilda E, Sridevi S. Formulation and evaluation of gastroretentive floating tablets of Gabapentin using Effervescent technology. Int J Pharm Biomed Res. 2012; 3(4):202-8.
13. Abul kalam lutful Kabir, Bishyajit kumar Biswas, Abu Shara shamsur Rouf. Design, Fabrication and evaluation of drug release kinetics from aceclofenac matrix tablets using HPMC. Dhaka University Journal of Pharmaceutical Sciences. 2009 Jun ;8 (1):23-30. DOI:<https://doi.org/10.3329/dujps.v8i1.5332>
14. Rubenstein et.al., "gastrointestinal physiological variables affecting the performance of oral SR dosage forms "in oral sustained release formulations: design and evaluation, Yaacob and E.H Walesa, Eds (Pergamon Press, New York)
15. Jeetendra Singh N, Vandana J, Nikhil K. Development of non-effervescent floating matrix tablets based on Euryale ferox seeds. Asian Journal of Pharmaceutics. 2011 Apr-Jun; 5: 93-100. DOI:10.4103/0973-8398.84549
16. Radke RS, Deshmukh SB, Jagtap PS, et al. Design and evaluation of gastroretentive floating tablets of captopril. IJPBS. 2010 Jan; V1(2):1-10.
17. Sameer S, Kalpana P, Pathak AK, Mishra A. Formulation and evaluation of floating tablet of captopril. International Journal of Pharm Tech Research. 2011 Jan-Mar; 3(1):333-41.
18. Brahmkar DM, Jaiswal SB. Biopharmaceutics and Pharmacokinetics. Vallabh Prakashan, Delhi. 2009; 2nd ed: pp.431-3.

