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Original Article

EFFECT OF PEANUT HUSK POWDER AS A NATURAL POLYMER IN THE FORMULATION AND EVALUATION OF GASTRO-RETENTIVE DRUG DELIVERY SYSTEM OF VALSARTAN FLOATING TABLETS

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ABSTRACT

Novel drug delivery system are becoming one of the most important fields in modern pharmaceuticals, formulation technology and several techniques are employed to design the sustained controlled drug delivery system. In the present study attempt has been made to develop sustained released drug delivery system by formulating the floating tablets of valsartan using peanut husk powder as a natural polymer (cellulose 35.7%, hemicelluloses 18.7%, lignin 30.2%) which is biodegradable, biocompatible, nontoxic, economically cheap cost, devoid of adverse and side effects and easily availability. Valsartan is effective as antihypertensive agent chemically N-(1-oxopentyl)-N-[[2-(1H-tetrazol-5-yl) [1, 1'-biphenyl]-4[-yl] methyl] L-valine.It has a half-life 6hrs, effective plasma concentration is (2-4) hours. The 9 batches of floating tablets (F-1 to F-9) were formulated by direct compression method using different ratio of polymers like peanut husk power, HPMC and carbopol. The formulated tablets were evaluated by means of different parameters like shape and density of tablet, hardness, friability, weight variation, drug content uniformity, *In vitro* buoyancy, swelling Index, *In vitro* dissolution studies. The formulation 5 has better sustained release when compared other formulations, it release the drug of about 40% at the 1st hr and almost 80% release at the end of 8hrs, hence we conclude that the combination of peanut husk powder, HPMC and carbopol shows better Gastric retention time which sustains the release of the dosage form.

INTRODUCTION

The oral controlled drug delivery systems (DDS) should be primarily aimed to achieving more predictable and increased bioavailability of drugs. However, the development process is precluded by several physiological difficulties, such as an inability to restrain and localize the DDS within the desired regions of the gastrointestinal (GI) tract and the highly variable nature of gastric emptying process. It can be anticipated that, depending upon the physiological state of the subject and the design of pharmaceutical formulation, the emptying process can last from a few minutes to 12 hours. This variability, in turn, may lead to unpredictable bioavailability and times to achieve peak plasma levels, since the majority of drugs are preferentially absorbed in the upper part of this small intestine. Furthermore, the relatively brief gastric emptying time (GET) in humans, which normally averages 2-3 hours through the major absorption zone (stomach or upper part of the

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intestine), can result in incomplete drug release from the DDS leading to diminished efficacy of the administered dose[1-5]. These considerations have lead to the development of oral controlled release (CR) dosage forms possessing gastric retention capabilities[1]. Prolonged gastric retention improves bioavailability, reduces drug waste, useful for drugs acting locally in the GIT, drugs which are poorly soluble and unstable in intestinal fluids. Recently, various efforts are being made to design gastro retentive systems such as, floating, swelling and expanding, bioadhesive/mucoadhesive, modified shape, low density/high density and raft systems etc. These systems are advantageous in improving GIT absorption of drug with CR due to specific site absorption limitations. Among the various gastro retentive systems, gastric floating drug delivery systems (GFDDS) offer numerous advantages over the gastric retentive systems. These systems have a density lower than the gastric fluids and thus remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period. While the system is floating on the gastric contents, the drug is released slowly at a desired rate from the stomach[6-8]. The gastro retentive drug delivery systems can be retained in the stomach and assist in improving the oral sustained delivery of drugs that have an absorption window in a particular region of the gastrointestinal tract. These systems help in continuously releasing the drug before it reaches the absorption window, thus ensuring optimal bioavailability[9-10].

⇨ **Criteria aimed to achieve**

1. Tablets should have satisfactory properties.
2. Tablet release more than 90% of drug within 8 hours.
3. Floating lag time of drug delivery system is reduced to minimum.
4. Tablet remains buoyant for 8 hours in stomach and releases the drug in controlled manner.

Valsartan is chemically N-(1-oxopentyl)-N-[[2-(1H-tetrazol-5-yl) [1,1'-biphenyl]-4[-yl] methyl] L-Valine which is used as an Anti-hypertensive agent and Angiotension 2 receptor antagonist. Valsartan is an angiotensin receptor blocker widely prescribed for hypertension. Valsartan blocks the actions of AngioTension 2, which include constricting blood vessels and activating aldosterone to reduce blood pressure. It is absorbed from the upper part of gastrointestinal tract. The oral bioavailability of Valsartan was reported to be 23% and largely present in unionized form in acidic pH. The recommended adult oral dosage of Valsartan is 80 mg for the effective treatment of hypertension. The short biological half-life of drug (6 hrs) also favors development of sustained release formulations. Drugs, which are easily absorbed from the gastrointestinal tract and those with short half-life, are quickly eliminated from the systemic circulation due to which frequent dosing is desired. To reduce this problem, gastro retentive drug delivery systems, which provide effective plasma drug concentration for longer periods thereby reducing the dosing frequency, are being formulated. It also has an advantage of minimizing the fluctuations in plasma drug concentration by delivering the drug in a controlled and reproducible manner[11-12]. Therefore, in the current study, floating tablets of valsartan were prepared using HPMC E50 and Carbopol 934 as the polymers, NaHCO3 as gas generating agent and Peanut husk powder as floating enhancer. The aim of the study was to evaluate the effect of Peanut husk powder on drug release and the effect of sodium bicarbonate on buoyancy.

MATRIALS AND METHODS:

Valsartan was used as the active ingredient was received as a gift sample from Microlabs Pvt. Ltd, Bangalore. HPMC K50 and Carbopol 934 were used as the polymers. Sodium bicarbonate was used a gas generating agent. The other ingredients used were magnesium stearate and Talc were purchased from Nice Chemicals Pvt. Ltd, Cochin. All reagents used were of analytical grade.

Preparation of gastro retentive floating tablets

Floating tablets contains valsartan were prepared by direct compression technique using variable concentrations of HPMC-E60 php powder, carbopol and talc with sodium bicarbonate Different tablets formulations were prepared by direct compression technique. All the powders were passed through 100 mesh sieve. Required quantity of drug, and low-density polymer were mixed thoroughly. Talc and magnesium stearate were finally added as glident and lubricant respectively. The blend was directly compressed (9mm diameter punches) using tablet compression machine. Each tablet contained 40mg of valsartan and other pharmaceutical ingredients as listed in table No1 in each section.

Evaluation of Floating tablets[13-17]:

Weight variation test

To study weight variation twenty tablets of the formulation were weighed using a Sartorius electronic balance and the test was performed according to the official method. Twenty tablets were selected randomly from each batch and weighed individually to check for weight variation.

Drug content

Five tablets were weighed individually and powdered. The powder equivalent to average weight of tablets was weighed and drug was extracted in 0.1 N HCl, the drug content was determined measuring the absorbance at 266.2 nm after suitable dilution using a Shimadzu UV-1601 UV/Vis double beam spectrophotometer.

Hardness

Hardness indicates the ability of a tablet to withstand mechanical shocks while handling. The hardness of the tablets was determined using Monsanto hardness tester. It is expressed in kg/cm^2. Three tablets were randomly picked and hardness of the tablets were determined.

Thickness

The thickness of the tablets was determined by using vernier calipers. Five tablets were used, and average values were calculated.

Friability Test

The friability of tablets were determined using Roche Friabilator. It is expressed in percentage (%). Ten tablets were initially weighed ($W_{initial}$) and transferred into friabilator. The friabilator was operated at 25rpm for 4 minutes or run up to 100 revolutions. The tablets were weighed again (W_{final}). The % friability was then calculated by –

$$\%F = 100\ (1\text{-}W_0/W)$$

% Friability of tablets less than 1% are considered acceptable.

Tablet Density

Tablet density is an important parameter for floating tablets. The tablet will float when its density is less than that of 0.1N HCL (1.004). The density was determined using following formula.

$$V = \pi r^2 h$$

$$d = m/v$$

v = volume of tablet (cc), r = radius of tablet (cm), h = crown thickness of tablet (cm) and m = mass of tablet

***In vitro* buoyancy studies**

The in vitro buoyancy was determined by floating lag time method described by Dave B.S. The tablets were placed in 250 ml beaker containing 0.1 N HCl. The time required for the tablets to rise to the surface and float was determined as floating lag time. The time between introduction of dosage form and its buoyancy in 0.1 N HCl and the time during which the dosage form remain buoyant were measured. The time taken for dosage form to emerge on surface of medium called Floating Lag Time (FLT) or Buoyancy Lag Time (BLT) and total duration of time by which dosage form remain buoyant is called Total Floating Time (TFT).

***In Vitro* dissolution studies**

The release rate of valsartan from floating tablets was determined using *The United States Pharmacopoeia* (USP) XXIV dissolution testing apparatus II (paddle method). The dissolution test was performed using 900 ml of 0.1 N HCl, at 37 ± 0.5°C and 75 rpm A sample (5 ml) of the solution was withdrawn from the dissolution apparatus hourly for 8 hours, and the samples were replaced with fresh dissolution medium. The samples diluted to a suitable concentration with 0.1N HCl. Absorbance of these solutions was measured at 248 nm using a Shimadzu UV-1601 UV/Vis double beam spectrophotometer. Cumulative percentage of drug release was calculated using the equation obtained from a standard curve.

Swelling index

The swelling index of tablets was determined n 0.1 N HCl (pH 1.2) at room temperature. The swollen weight of the tablets was determined at predefined time intervals. The swelling index was calculated by the following equation:

$$\text{Swelling index WU} = \frac{(W_1 - W_0)}{W_0} \times 100$$

Where, W_t = Weight of tablet at time t and W_0 = Initial weight of tablet

RESULTS & DISCUSSION:

Hydrodynamically balanced tablets of Valsartan (gastroretentive drug delivery systems) were prepared and evaluated to increase its local action and bioavailability In the present study 9 formulations with variable concentration of polymer were prepared and evaluated for physiochemical parameters, invitro buoyancy studies, invitro release studies.

Compatibility studies:

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. In the present study, it has been observed that there is no chemical interaction between Valsartan and the polymers used.

Table No 1: Composition of valsartan floating tablets (Batches F1 to F9)

Ingredients	FT1	FT2	FT3	FT4	FT5	FT6	FT7	FT8	FT9
Valsartan	80	80	80	80	80	80	80	80	80
PH powder	35	35	-	35	70	70	175	-	-
HPMC E50	140	-	140	70	70	35	-	175	-
Carbopol	-	140	35	70	35	70	-	-	175
Sodium bicarbonate	25	25	25	25	25	25	25	25	25
Magnesium Stearate	10	10	10	10	10	10	10	10	10
Talc	10	10	10	10	10	10	10	10	10

Table no 2: Evaluation data for batches F1 to F9

S.No	Batches	Thickness (mm)	Diameter (mm)	Hardness	Friability In %	Floating time in hrs	Drug concen-tration in %
1	F-1	4.032	13.58	2.6	0.5	12.00	100.45
2.	F-2	4.030	13.54	3.2	0.3	10.00	099.40
3.	F-3	4.025	13.50	3.2	0.3	10.30	098.40
4.	F-4	4.032	13.58	2.8	0.4	12.00	100.70
5.	F-5	4.034	13.60	3.0	0.4	11.00	099.80
6.	F-6	4.030	13.54	3.0	0.5	10.45	099.70
7.	F-7	4.025	13.50	3.8	0.3	14.00	100.65
8.	F-8	4.027	13.52	3.4	0.2	09.00	O99.10
9.	F-9	4.032	13.58	3.6	0.4	12.30	100.55

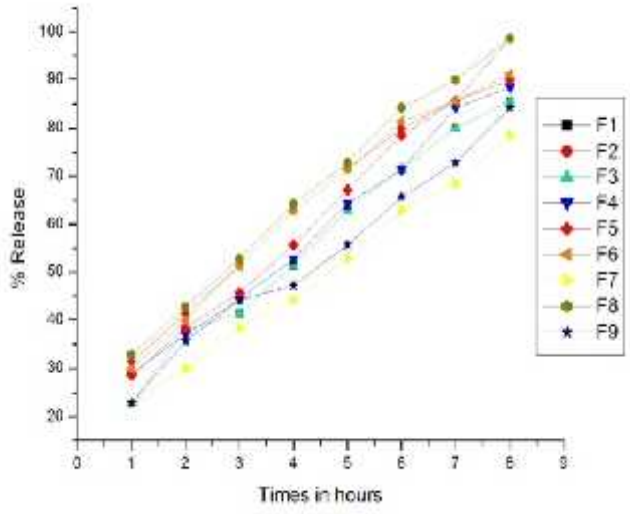

Fig no 1: *In vitro* drug release of batches F1 to F9

It was observed that there were no changes in these main peaks in IR spectra of mixture of drug and polymers, which show there were no physical interactions because of some bond formation between drug and polymers. The peaks obtained in the spectra's of each formulation correlates with the peaks of drug spectrum. This indicates that the drug was compatible with the formulation components. The formulated floating tablets were evaluated in terms of different parameters like thickness, diameter, hardness, friability, floating lag time, buoyancy, drug content and *in vitro* drug release, the results of evaluation parameters were tabulated in the table no 2.

In vitro Drug Release:

From the *in-vitro* dissolution data it was found that formulation FT1, FT2. FT3, FT4, FT5, FT6, FT7 and FT9 released more than 90% of drug before 8 hr of the study indicating that the polymer amount is not sufficient to control the drug release. While FT 1 and FT 9 containing all polymers released more than 90% of drug with in 8 hr. It concludes FT

5 had better controlled release than the other formulation.

CONCLUSION:

The floating time range from 8hours to 14hours and the swelling index of different formulation ranged for thickness from 12.74% to 55.03% and for diameter 1.78% to 16. %. Formulation 1 showed a release of about 22% at the first hour and almost complete release at end of 8 hour. Formulation 2&3 showed a release of about 31% at the first hour and almost complete release at end of 8hour. Formulation 4 showed a release of about 28% at the first hour and almost complete release at end of 8hours. Formulation 5 showed a release of about 40%at the first hour and almost complete at only around 80% release end of 8hours. Formulation 6&7 showed a release of about 22% at the end of first hour and only around 80% release at the end of 7hours and formulation 8&9 showed a release of about 32% at the end of the first hour and only around 90% at the end of 7 hours. From the 9 different formulations we find that the formulation contain combination of Peanut Husk powder, HPMC and Carbopal (i.e F5) were better sustained release when compared the other formulations.

REFERENCE:

1. Somwanshi BS and Dolas TR. Floating multiparticulate oral sustained release drug delivery system. Journal of Chemical and Pharmaceutical Research. 2011;3(1):547-536.
2. Sharma M, A Review on Floating Multiparticulate System for Gastric Retention. American Journal of Pharmatech Research. 2012;2(6):149-126.
3. Dhole AR, A Review on Floating Multiparticulate Drug Delivery System: A Novel Approach to Gastric Retention. International Journal of Pharmaceutical Sciences Review and Research. 2011; 6(2):211-205.
4. Chikhalikar, Floating Drug Delivery System: An Approach to Oral Controlled Drug Delivery. International Journal of Pharm Tech Research. 2012; 4(4):1826-1812.
5. *Patel N Ara*, Formulation and characterization of floating tablets of diltiazem hydrochloride*, jpbms, 2011, 9 (21).*
6. Gandhi B and Baheti J. Multiparticulates Drug Delivery Systems: A Review. International Journal of Pharmaceutical and Chemical Sciences. 2013;2(3):1626-1620.
7. Sirisha VR and Sri VK. A Review of Pellets and Pelletization Process: A Multiparticulate Drug Delivery System. International Journal of Pharmaceutical Sciences and Research. 2013;4(6): 2158-2150.
8. Ravi kumar, M. B. Patil., "Formulation and evaluation of effervescent floating tablet of Famotidine", Int. J. Pharm., 2009 vol.1, no.3, pp 754-763 ,
9. Kondivanitha,"Formulation and *in-vitro* evaluation of floating tablets of hydralazine hydrochloride", Int. J. Pharm., 2012, pp 51-58.
10. N Arunkumar, "Formulation and *in vitro* evaluation of oral floating tablets of atorvastatin calcium", Int. J. Pharm., *2008, 492-495.*
11. C.P. Jain1," Formulation and evaluation of fast dissolving tablets of valsartan", Int. J. Pharm., 2009., 219-226
12. K.Kannan, Development and evaluation of valsartan film coated tablets", J. Pharm. Sci. & res. Vol.4 (6), 2012, 1866 – 1871.
13. Chandra sekhararao. Formulation and evaluation of floating matrix tablets of ramipril using peanut husk powder, *ijpd, 3(2), 2013, 72-79.*
14. Chandra Sekhara Rao G, Formulation and evaluation of floating matrix tablets of ramipril using peanut husk powder, International Journal of Pharmaceutical Development & Technology, 2013; 3(2): 72-79.
15. Radke RS, et al. Design and evaluation of gastroretentive floating tablets of captopril. *IJPBS*, V1(2), 2010, 1-10.
16. Streubel A, Siepmann J, Bodmeier R. Floating matrix tablets based on low density foam powder: effects of formulation and processing parameters on drug release. *European Journal of Pharmaceutical Sciences*, 18, 2003, 37-45.
17. Jeetendra Singh N, Development of non-effervescent floating matrix tablets based on *Euryale ferox* seeds. *Asian Journal of Pharmaceutics*, 2011, 93-9.

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