IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

GASTRO-RETENTIVE DRUG DELIVERY SYSTEM OF HYPERTENSION DRUG: FORMULATION AND EVALUATION STUDIES

Robin Bhilwal*, Bharat K. Tyagi

Master of Pharmacy (Research Scholar) , Department of Pharmaceutical Science.

Institute of Professional Studies College of Pharmacy, Gwalior, Madhya Pradesh, India

Abstract: The current study aims to develop gastro-retentive drug delivery systems for hypertension medication development and evaluation. The primary goal of oral controlled drug delivery systems (CDDS) should be to achieve more predictable and enhanced medication bioavailability. The design process, however, is hampered by a number of physiological challenges, including the inability to constrain and localise the CDDS within the targeted parts of the gastrointestinal (GI) tract and the extremely changeable nature of the stomach emptying process. Preparation and testing of a floating Candesartan tablet based on a low density polymer that keeps the dosage form in the gastrointestinal.Using HPMC K15M, HPMC K50M, and Ethyl cellulose as sustain release polymers, provide an enhanced stomach residence duration, resulting in prolonged drug delivery in the gastrointestinal system. To investigate the many formulation and process variables that influence pharmaceutical drug release.

Keyword **– Candesartan, Floatin Tablet, Formulation, Evaluation, Gastrointestinal .**

I. INTRODUCTION

The most convenient and favoured method of drug delivery to the systemic circulation is oral administration.Controlled by mouthrelease medicine delivery has recently gained popularity to boost therapeutic benefits in the pharmaceutical business, such as dosage administration convenience, patient compliance, and formulation adaptability Drugs that are easily absorbed from the body. These are eliminated from the gastrointestinal tract (GIT) and have short half-lives. Rapidly from systemic circulation Frequent administration of these to achieve appropriate therapeutic activity. Medicines are requiredIn order to avoid to overcome this constraint. Following oral administration, such a drug delivery would be held in the stomach and release the medication in a controlled manner, allowing the drug to be released in a controlled manner.The medicine might be continually delivered to its absorption sites in the GIT stands for gastrointestinal tract. These drug delivery methods face primarily two challenges: the unanticipated short gastric retention time (GRT) gastric emptying time (GET), which can lead to inadequate medication absorptionrelease of the dose form in the absorption zone (stomach or intestines)upper section of the small intestine), resulting in decreased efficiency ofdose that was given To create a site-specific orally delivered medication. It is preferable to use a controlled release dose form to provide a longer duration of action.

II. MATERIAL AND PROCEDURES

Pharmaceutical kindly purchased Candesartan Mumbai Laboratories Ltd. orthophosphate of potassium dihydrogen Disodium hydrogen orthophosphate and sodium hydrogen orthophosphate were obtained from Ethanol, methanol, and acetone were used by Colorcon Pvt. Ltd. in Goa.Bought from Industry of Ranbaxy Fine Chemical Ltd., New Delhi.

Preformulation Study

It is one of the important prerequisite in development of any drug delivery system. Preformulation studies were performed on the drug, which included melting point determination, solubility and compatibility studies.

Formulation of Gastro-Retentive floatingTablets

Floating tablets containing Candesartan Cilexetil were prepared by direct compression technique using variable concentrations of HPMC K15M, HPMC K50M, and Ethyl cellulose with sodium bicarbonate.Different tablet formulation were prepared by direct compression method .All the powders were passed through 60 mesh sieve the required qty. of drug and lower density polymer were mixed geometrically and then tablets are compressed in compression machine at specified pressure

with 11 mm round punch.

Determination of MeltingPoint

Melting point of Candesartan was determined by capillary method. Fine powder of Candesartan was filled in glass capillary tube (previously sealed on one end). The capillary tube is tied to thermo meter and the thermometer was placed in fire. The powder at what temperature it will melt, was noticed.

Solubility

Solubility of Candesartan was determined in ethanol (95%), chloroform, acetone, ether, water and 0.1 N HCl. Solubility studies were performed by taking excess amount of Candesartan in different beakers containing the solvents. The mixtures were shaken for 24 hrs at regularintervals. Whattmann's filter paper grade no. 41 was used to filtrate the solutions. The filtrate solutions are spectrophotometrically examined.

Compatibility Studies

IR experiments were performed to confirm excipient compatibility. IR tests were performed on the purified medication, its formulation, and excipients.

In vitro buoyancy studies

The floating lag time method described by Dave B.S. was used to measure in vitro buoyancy. The tablets were dropped into a 250 ml beaker with 0.1 N HCl. The floating lag time was calculated as the time it took for the tablets to rise to the surface and float. The time between the introduction of the dosage form and its buoyancy in 0.1 N HCl, as well as the duration the dosage form remained buoyant, were measured. The time it takes for the dosage form to emerge on the surface of the medium is known as Floating Lag Time (FLT) or Buoyancy Lag Time (BLT), and the overall period of time the dosage form remains buoyant is known as Total Floating Time (TFT).

Swelli gindex

The swelling index of tablets was measured at room temperature using 0.1N HCl (pH 1.2). The expanded weight of the tablets was determined at regular intervals.

III. RESULTS AND DISCUSSION

Preformulation Characters

The physical characterization of the drug was performed according to the reported procedure and the results obtained were compared with that of the standard curve.(Table 1.)

The hydrodynamic balancing system (HBS), also known as the Floating drug delivery system (FDDS), is an oral dosage form (capsule or tablet) that is meant to extend the dosage form's residence period within the GIT. It is a medication formulation containing gel-forming hydrocolloids designed to float in the stomach contents. Under relatively controlled conditions, drug disintegration and release from the dosage form stored in stomach fluids happens at the pH of the stomach.

Candesartan Cilexetil hydrodynamically balanced tablets (gastro retentive drug administration techniques) were designed and tested to improve local action and bioavailability. In this work, ten formulations with varying polymer concentrations were developed and tested for physicochemical parameters, in-vitro buoyancy studies, in-vitro release studies, and stability investigations. The prepared batches were displayed in (Table. 2).

Compatibility testing were carried out using an infrared spectrophotometer. The infrared spectra of a pure drug as well as a physical mixture of drug and polymers were investigated. Candersartan Cilexetil peaks were observed at 1701 c.m-1, 1591 c.m-1, 1435 c.m-1, 1280 c.m-1, 1070 c.m-1, 960 c.m-1, 702 c.m-1, and 690 c.m-1. Interactions between drugs and excipients, among other things, influence drug release from formulations. This study found that there is no chemical interaction between Candersartan Cilexetil and the polymers used. 1..1, 1.2, 1.3, and 1.4 Figures In the IR spectra of the drug and polymer combination, there were essentially no changes in these important peaks, indicating that there were no physical interactions owing to bond formation between the drug and polymer. Peaks in the spectra of each polymer correspond to peaks in the pharmacological spectrum. This indicates that the drug was suitable with the chemicals.

Standard calibration curve of candersartan Cilexetil

A pharmaceutical solution is scanned in the UV range (200-400 nm) to find the highest absorption wavelength (max). The maximum wavelengths were discovered to be 258.2 nm and 260.8 nm. The Candersartan Cilexetil Standard calibration curve was created at these wave lengths. The calibration curve was linear between 2 and 12 g/ml concentration ranges. Candersartan Cilexetil's standard calibration curve was determined by graphing absorbance vs concentration at 260.8 nm and 258.2 nm in both phosphate buffer and 0.1i N HCl, and it follows Beer's law. Table 4 summarises the findings. (2.1.a) and (2.1.b) figures (2.1.b). The r2 and slope in phosphate buffer were 0.9994 and 0.0774, respectively, while in 0.1 N Hcl, they were 0.9976 and 0.0198.

In vitro Buoyancy Study

On immersion in 0.1N HC solution pH (1.2) at 37°C, the tablets floated, and remained buoyant without disintegration. Table 3. shows the results of Buoyancy study. According to the results, the batch comprising just HPMC polymer demonstrated good Buoyancy lag time (BLT) and Total floating time (TFT). The formulation including HPMC K15M, HPMC K50M, and Ethyl cellulose had a decent BLT of 52 seconds, however the formulation having Ethyl cellulose alone did not float for more than 80 minutes.

IV. CONCLUSION

The compatibility studies revealed that HPMC K15M, HPMC K50M, and Ethyl cellulose were compatible with Candesartan Cilexetil and hence suitable for the formulation of Candesartan Cilexetil floating tablets. All formulations, from FT 1 to FT 10, were buoyancy evaluated in vitro at 37oC using a 0.1 N HCl solution. With the exception of FT 3 and FT 6, all formulas were floated. The formulation FT 7 had a longer floating period (12 hours) than the other formulations since it contains 90 mg of HPMC K15M, 45 mg of HPMC K50M, and 45 mg of Ethyl cellulose.

V. REFERENCES

- R. Bomma et.al : Development and evolution of gastro retentive norfloxacin tablets Acta Pharma 59(2009)211-221.
- V.T. Thakkar et.al.fabrication & evaluation of levofloxacin hemihydrate floating tablet research in pharmaceutical sciences 2008 3(2) :1-8.
- B. Prakash Rao Neelima Ashok Kottan Snehit vs, Ramesh Development of Gastro retentive drug delivery system of cephalexin by using factorial design ARS pharmaceutica 2009 Vol. 50,8-24.
- Whitehead L, Collett JH, Fell JT. Amoxycillin release from a floating dosage form based on alginates. Int J Pharm2000;210:45-9.
- Dollery C Therapeutic drugs. London: Churchill Livingstone: 1991. vol 2 p.25 - 7.
- The British Pharmacopoeia. London:The Pharmaceutical Press:2002.p.1003-4.
- Sridevi S, Diwan PVR. Optimized transdermal delivery of ketoprofen using pH and hydroxypropyl-β-cyclodextrin as coenhancers. Eur J Pharm Biopharm 2002;54:151-4.
- Green GA. Understanding NSAIDs: from aspirin to COX-2. Clin Cornerstone 2001;3:50-9.
- KantorTG.Ketoprofen:areviewofitspharmacologicandclinicalproperties.Pharmacotherapy. 1986;93 -103.
- Vavra. AJ, Lewis DE. Ketoprofen. in nonsteroidal anti-inflammatory drugs. 1st ed New York: Marcel Dekker; 1987. p.419 -37.
- Sweetman SC, Martindale. The Complete Drug Reference. 33rd ed London: The Pharmaceutical Press; 2002. p.47 -8.
- Roche RC., Sheskey PJ, Weller PJ. Handbook of pharmaceutical excipients. 4th ed London: Pharmaceutical Press;2003.
- Cooper J, Gun C, Carter SJ Powder Flow andCompaction.Tutorial Pharmacy.New Delhi: CBS Publishers; 1986. p.211-33.
- Martin A, Baltimores MD. Micromeretics physical pharmacy. London: Lippincott Williams and Wilkins; 2001.p.423-54.
- Chaudhri PD, Chaudhri SP, Kolhe SR. Formulation and evaluation of fast dissolving tablets of famotidine. Indian Drugs2005;42(10):641-7.
- Rouge N, Buri P, Doelker E. Drug absorption sites in the gastrointestinal tract and dosage forms for site-specific delivery. Int J Pharm1996;136:117-39.
- ReddyL,MurthyR. Floa ting dosage systems in drug delivery.Crit Rev The rDrug Carrier Syst2002;19:553-85.
- Deshpande AA, Shah NH, Rhodes CT, Malick W. Development of a novel controlled release system for gastric retention. Pharm Res1997;14:815-9.
- Sheth PR, Tossounian J. The hydrodynamically balanced system (HBS ™) : a novel drug delivery system for oral use. Drug Dev Ind Pharm1984;10:313-39.
- Gutierrez-rocca J, Omidian H, Shah K. Progress in Gastroretentivedrugdelivery systems. Business Briefing, Pharmatech 2003;152-6.
- Hou SY, Cowles VE, Berner B. Gastric retentive dosage forms: a review. CritRev Ther Drug Carrier Syst2003;20(6):459-97.
- Chatterjee CC. Human Physiology. Vol I, Medical Allied Agency; Kolkata; 2004; 435-38.
- Waugh A, Grand A. Ross and Wilson Anatomy and Physiology: In Health and Illness.10th edi, Churchill Livinstone Elsevier; Edinburgh; 2006;293-95.
- CheinYW. Novel Drug Delivery Systems,2nd edition,MarcelDekker,NewYork, 2005,157-63.

Table 1. Standard Curve of Candesartan Cilexetil

S.NO	*CONCENTRATION (µg/ml)*	*ABSORBANCE In HCL*	*ABSORBANCE In Phosphate buffer(7.4)*
1.	0	0	0
2.	2	0.038	0.153
3.	4	0.0646	0.320
4.	6	0.116	0.480
5.	8	0.165	0.614
6.	10	0.191	0.770
7.	12	0.238	0.936
		Y=.0.0198 R^2 0.9976	Y=0.0774 R^2 0.9994

Table 2. Composition of Candesartan Cilexetil Floating Tablets

INGREDIENTS	FT1	FT2	FT3	FT4	FT5	FT6	FT7	FT8	FT9	FT10
Candesartan Cilexetil	200	200	200	200	200	200	200	200	200	200
HPMC K15M	180	-	-	90	90	-	90	45	45	60
HPMC K50M	-	180	-	90	-	90	45	90	45	60
Ethyl cellulose	-	-	180	-	90	90	45	45	90	60
Sodium bicarbonate	80	80	80	80	80	80	80	80	80	80
Citric acid (anhydrous)	20	20	20	20	20	20	20	20	20	20
PVP-K-30	25	25	25	25	25	25	25	25	25	25
Magnesium Stearate	8	8	8	8	8	8	8	8	8	8
Talc	7	7	7	7	7	7	7	7	7	7

Table 3. Effect of hardness on Buoyancy Lag Time

Hardness in kg/cm^2	Buoyancy Lag Time (sec)
4	52
5	61
6	79
7	94
8	190

Table 4. Evaluation of Physical Parameters of Floating Tablets					
Tablets Batch	**Weight variation test (%)**	**Friability (%)**	**Hardness (kg/cm^2)**	**Thickness (mm)**	**Drug Content (%)**
FT1	± 1.75	0.37	5.9 ±0.47	4.04 ± 0.2	98.50
FT2	±3.52	0.76	4.6 □0.72	4.12 □0.015	97.05
FT3	±2.15	0.56	4.8 □1.29	4.19 □0.017	98.4
FT4	±1.56	0.76	5.4 □0.28	4.13□0.06	97.25
FT5	±3.54	0.59	6.2□0.45	4.14 □0.11	96.42
FT6	±1.42	0.70	4.5□0.29	4.15 □0.012	98.29
FT7	±2.11.	0.56	4.2 □0.64	4.12 □0.014	99.85
FT8	±1.89	0.79	5.2 □0.24	4.13 □0.016	98.44
FT9	±2. 56	0.93	5.7 □0.28	4.06 □0.012	99.74
FT10	±2.04	0.67	5.4□0.86	4.08□0.011	98.40

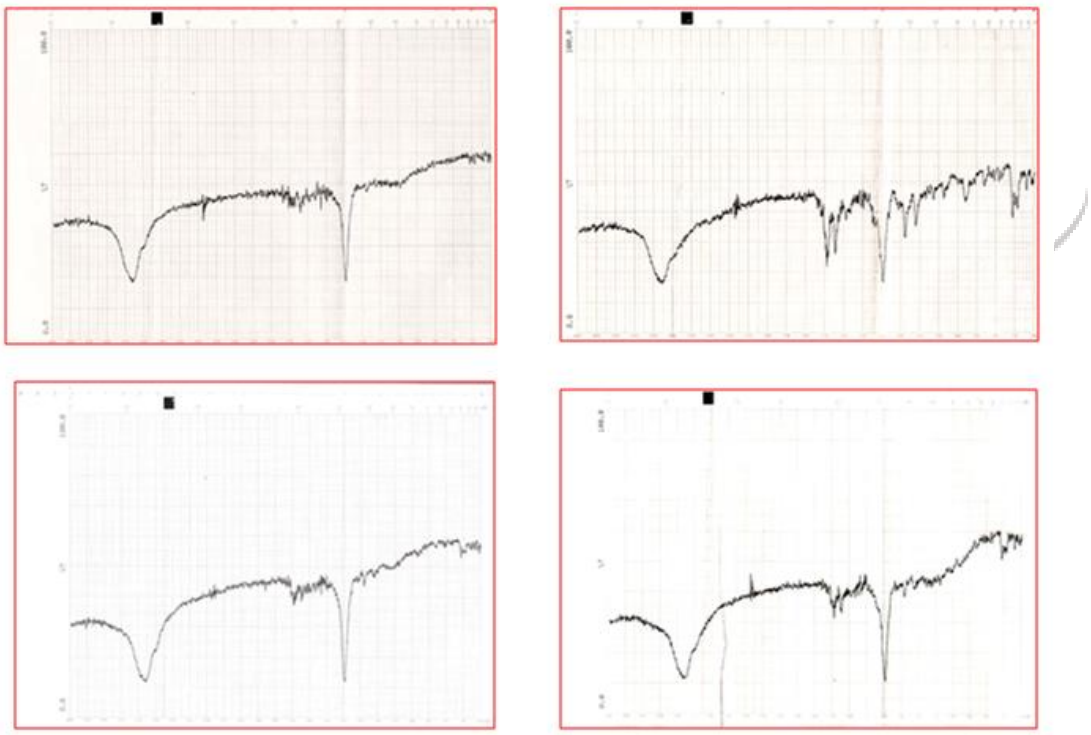
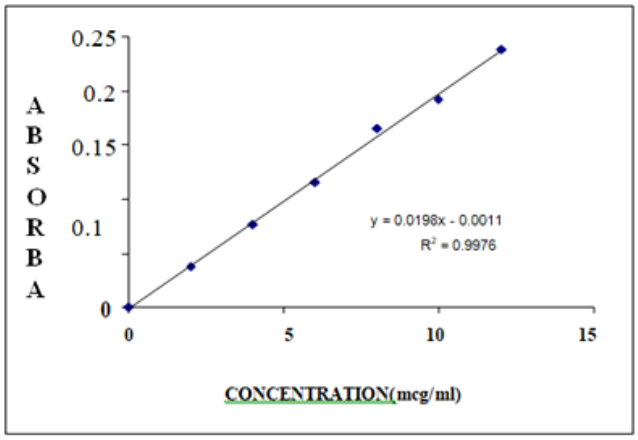


Figure 1. I.R. Spectrum of Candesartan Cilexetil



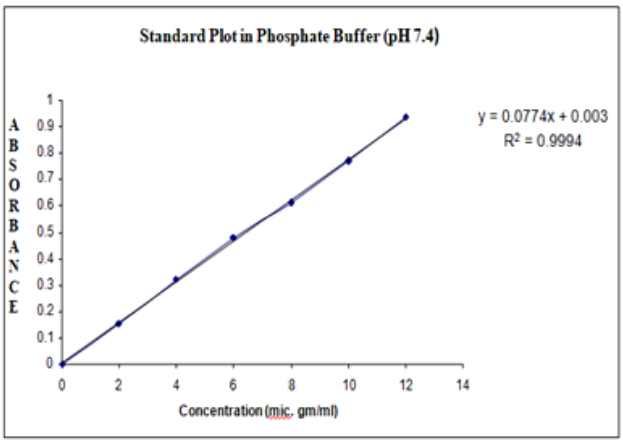


Figure 2. Standard calibration curve of valsartan in 0.1n hclfigure 2.1 (a),(b)