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Formulation and evaluation of floating tablets of esomeprazole

D.Sumith Reddy*[1], Ganesh Kumar Gudas[1]

[1]*Department of Pharmaceutics, Srikrupa Institute of Pharmaceutical Sciences, Siddipet,*

***Corresponding Author: D.Sumith Reddy**
Email: ganeshpharmaco@gmail.com

ABSTRACT

The present study outlines a systematic approach for designing and development of Esomeprazole floating tablets to enhance the bioavailability and therapeutic efficacy of the drug. Floating tablets of Esomeprazole have shown sustained release thereby proper duration of action at a particular site and are designed to prolong the gastric residence time after oral administration. Different formulations were formulated by using wet granulation technique. A floating drug delivery system (FDDS) was developed by using sodium bicarbonate as gas-forming agent and chitosan, compritol 888ato, HPMC K15 M as polymers. The prepared tablets were evaluated in terms of their physical characteristics, precompression parameters, in vitro release and buoyancy lag time. The results of the in vitro release studies showed that the optimized formulation (F6) could sustain drug release for 12 hrs by using HPMC K15M in the concentration of 60 mg. The in vitro drug release followed zero order kinetics. The stability of optimized formulation (F6) was known by performing stability studies for three months at accelerated condition of 40^0C±75%RH on optimized formulation. The F6 formulation was found to be stable with no change.

Keywords: Esomeprazole, HPMC K15 M and Floating tablets.

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 form. Oral route is considered most natural, uncomplicated, convenient and safe due to its ease of administration, patient acceptance and cost-effective manufacturing process [1].

Gastro retentive Dosage Form (GRDF)

It is evident from the recent scientific and patient literature that an increased interest in novel dosage forms that are retained in stomach for a prolonged and predictable period of time exists today in academic and industrial research groups. One of the most feasible approaches for achieving a prolonged and predictable drug delivery in the GI tract is to control the gastric residence time (GRT),

i.e. gastro retentive dosage form (GRDFs or GRDS) [2].

GRDFs extend significantly the period of time over which the drugs may be released. They not only prolong dosing intervals, but also increase patient compliance beyond the level of existing controlled release dosage form [3].

MATERIALS AND METHODS

Materials

Esomeprazole was obtained as a gift sample from HETERO LABS, Hyderabad, INDIA. Chitosan, Compritol 888 ATO, Hydroxy propyl methyl cellulose K15M, Sodium bicarbonate, Magnesium stearate, Micro crystalline cellulose, Talc were from Merck Specialities Pvt Ltd, Mumbai, India. All the chemicals and solvents used were of analytical grade.

Methods

Development of Spectrophotometric method

Determination of absorption maxima

A solution containing the concentration 10 µg/ ml drug was prepared in 0.1N HCl UV spectrum was taken using Double beam UV/VIS spectrophotometer. The solution was scanned in the range of 200 – 400.

Preparation calibration curve

100mg of Esomeprazole pure drug was dissolved in 100ml of 0.1N HCl (stock solution) 2ml of solution was taken and make up with 100ml of 0.1N HCl (20µg/ml). The above solution was subsequently diluted with 0.1N HCl to obtain series of dilutions Containing 2, 4, 6, 8, 10 and 12µg/ml of Esomeprazole per ml of solution. The absorbance of the above dilutions was measured at 266 nm by using UV-Spectrophotometer taking 0.1N HCl as blank. Then a graph was plotted by taking Concentration on X-Axis and Absorbance on Y-Axis which gives a straight line Linearity of standard curve was assessed from the square of correlation coefficient (R^2) which determined by least-square linear regression analysis [4].

FORMULATION DEVELOPMENT OF TABLETS

All the formulations were prepared by wet granulation. The tablets were prepared as per the procedure given below and aim is to prolong the release of Esomeprazole. Total weight of the tablet was considered as 150 mg.

Procedure

Esomeprazole and all other ingredients were individually passed through sieve no □ 60. All the ingredients were mixed thoroughly by triturating up to 15 min. 10%w/v starch solution binding agent was prepared. Starch solution was mixed with powder mixture to form wet mass. Wet mass was passed through the sieve no#18 to form granules. The granules were dried in hot air oven at 600 c for 50 minutes and passed through sieve no # 22. The granules were lubricated with talc and magnesium sterate. The tablets were prepared by using compression method.

Evaluation of post - compression parameters for prepared Tablets

The designed compression tablets were studied for their physicochemical properties like weight variation, hardness, thickness, friability and drug content [5].

Weight variation test

To study the weight variation, twenty tablets were taken and their weight was determined individually and collectively on a digital weighing balance. The average weight of one tablet was determined from the collective weight. Not more than two of the individual weights deviate from the average weight by more than the percentage shown in the following table and none deviate by more than twice the percentage. The mean and deviation were determined. The percent deviation was calculated using the following formula [6].

% Deviation = (Individual weight – Average weight / Average weight) × 100

Hardness

Hardness of tablet is defined as the force applied across the diameter of the tablet in order to break the tablet. The resistance of the tablet to chipping, abrasion or breakage under condition of storage transformation and handling before usage depends on its hardness. For each formulation, the

hardness of three tablets was determined using Monsanto hardness tester and the average is calculated and presented with deviation [7].

Thickness

Tablet thickness is an important characteristic in reproducing appearance. Tablet thickness is an important characteristic in reproducing appearance. Average thickness for core and coated tablets is calculated and presented with deviation.

Friability

It is measured of mechanical strength of tablets. Roche friabilator was used to determine the friability by following procedure. Preweighed tablets were placed in the friabilator. The tablets were rotated at 25 rpm for 4 minutes (100 rotations). At the end of test, the tablets were re weighed, loss in the weight of tablet is the measure of friability and is expressed in percentage as

% Friability = [(W1-W2) / W] × 100

Where, W1 = Initial weight of three tablets

W2 = Weight of the three tablets after testing

Determination of drug content

Prepared core tablets were subjected for the drug content. Twenty tablets were finely powdered, quantity of the powder equivalent to one tablet weight of Esomeprazole were accurately weighed, transferred to a 100-ml volumetric flask containing 50 ml water and allowed to stand to ensure complete solubility of the drug. The mixture was made up to volume with water. The solution was suitably diluted and the absorption was determined by UV –Visible spectrophotometer [8].

In vitro Buoyancy studies

The in vitro buoyancy was determined by floating lag time, and total floating time. (As per the method described by Rosa et al) The tablets were placed in a 100ml beaker containing 0.1N HCl. The time required for the tablet to rise to the surface and float was determined as floating lag time (FLT) and duration of time the tablet constantly floats on the dissolution medium was noted as Total Floating Time respectively (TFT) [9].

In vitro drug release studies

Procedure

900ml 0f 0.1 HCl was placed in vessel and the USP apparatus –II (Paddle Method) was assembled. The medium was allowed to equilibrate to temp of 37°c $\pm$ 0.5°c. Tablet was placed in the vessel and the vessel was covered the apparatus was operated for 12 hours and then the medium 0.1 N HCl was taken and process was continued from 0 to 12 hrs at 50 rpm. At definite time intervals of 5 ml of the receptors fluid was withdrawn, filtered and again 5ml receptor fluid was replaced. Suitable dilutions were done with receptor fluid and analyzed by spectrophotometrically at 266 nm using UV-spectrophotometer [10].

Accelerated stability studies

The optimized formulation was subjected to stability studies at 40^{o}C±75% RH for period of three months. Each tablet was individually wrapped in aluminium foil and packed in ambered coloured bottle and put at above specified condition in a heating humidity chamber for three months. For every one-month tablets were analysed for the hardness, friability, thickness, drug content and *in vitro* drug release [11].

RESULTS AND DISCUSSION

The present study was aimed to develop gastro retentive floating tablets of Esomeprazole using various natural polymers. All the formulations were evaluated for physicochemical properties and invitro drug release studies.

Calibration curve

Graphs of Esomeprazole was taken in Simulated Gastric fluid (pH 1.2) at 266 nm.

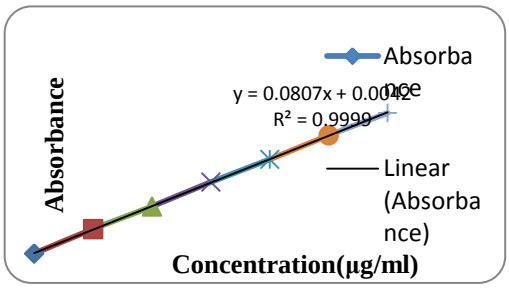

Fig.No.1: Standard graph of Esomeprazole in 0.1N HCl

The calibration curve showed linearity in the range of 2-12 microgram/ml. Regression co-efficient value was found to be 0.999 and slope value was found to be 0.08.

Quality Control Parameters For tablets

Tablet quality control tests such as weight variation, hardness, and friability, thickness, and drug release studies in different media were performed on the tablets.

Tablets were subjected to various quality control parameters. The weight variation of all the formulations was found to be in the range of 145.6±0.4 to 162.5±0.2 (mg). The hardness of all the formulations was found to be in the range of 4.1±0.7 to 4.5±0.8 (kg/cm2). The friability of all the formulations was found to be ranging between 0.45±0.4 to 0.55±0.2. The thickness of all the formulations was found to be in the range of 4.4±0.4 to 4.9±0.2. The drug content, floating lag time was found to be within the limits.

Table No.2: *Invitro* quality control parameters for tablets

Formulation code	Weight variation (mg)	Hardness (kg/cm2)	Friability (%loss)	Thickness (mm)	Drug content (%)	Floating lag time (min)	Floating time (hrs)
F1	162.5±0.2	4.5±0.8	0.52±0.9	4.8±0.9	99.76±0.2	4.0±0.5	<10
F2	155.4±0.7	4.2±0.2	0.54±0.8	4.9±0.5	99.45±0.8	4.2±0.2	<11
F3	148.6±05	4.4±0.7	0.51±0.2	4.9±0.4	99.34±0.2	4.5±0.8	<10
F4	145.6±0.4	4.5±0.5	0.55±0.7	4.9±0.2	99.87±0.9	4.1±0.9	<11
F5	153.4±0.5	4.4±0.4	0.56±0.2	4.7±0.7	99.14±0.2	4.0±0.8	<11
F6	154.7±0.8	4.2±0.2	0.45±0.4	4.5±0.5	98.56±0.7	4.4±0.2	>12
F7	152.3±0.2	4.1±0.7	0.51±0.5	4.4±0.4	98.42±0.2	4.5±0.7	<11
F8	151.2±0.9	4.3±0.2	0.49±0.7	4.7±0.2	99.65±0.7	4.6±0.5	<10
F9	148.3±0.8	4.5±0.4	0.55±0.2	4.6±0.7	99.12±0.5	4.7±0.4	<11

All the values are represented as Mean ± SD (n=3)

In-Vitro Drug Release Studies

The formulation of Esomeprazole floating tablets with synthetic carriers (chitosan, compritol 888 ato, HPMC K15M) were studied for the dissolution. The Esomeprazole with carrier HPMC K15M showed a marked increase in the dissolution rate in 0.1 N HCl. The F6 formulation showed maximum dissolution of 97.57% at 12hrs and proving that increased gastric residence time and thereby a longer period of drug delivery in GI tract. From the dissolution data it was evident that the formulation (F6) prepared with HPMC K15 M of concentration 60mg shown maximum drug release of 97.57 in 12 hours.

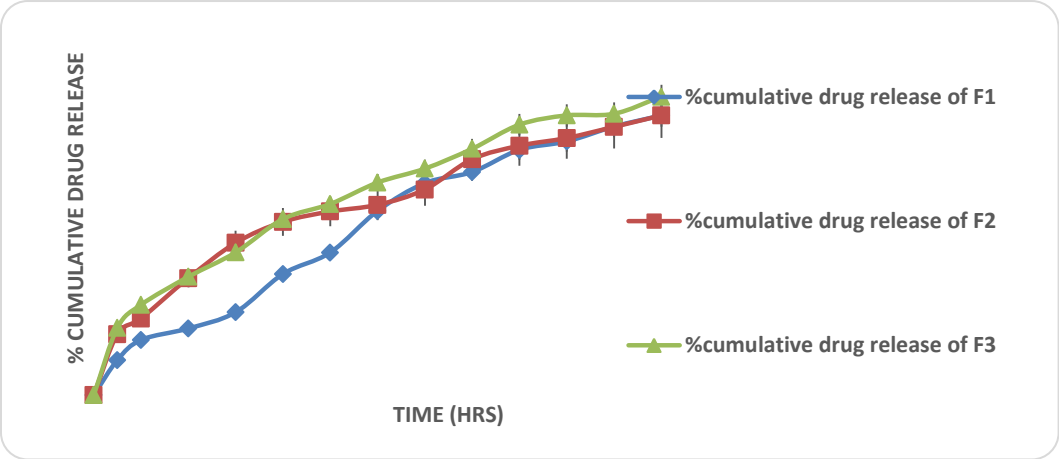

Fig.No.2: Dissolution profile of Esomeprazole floating tablets (F1, F2, F3 formulations)

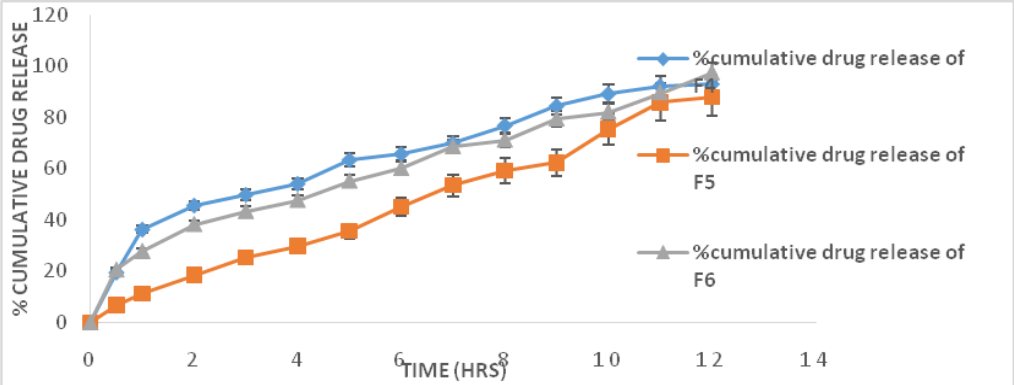

Fig.No.3: Dissolution profile of Esomeprazole floating tablets (F4, F5, F6 formulations)

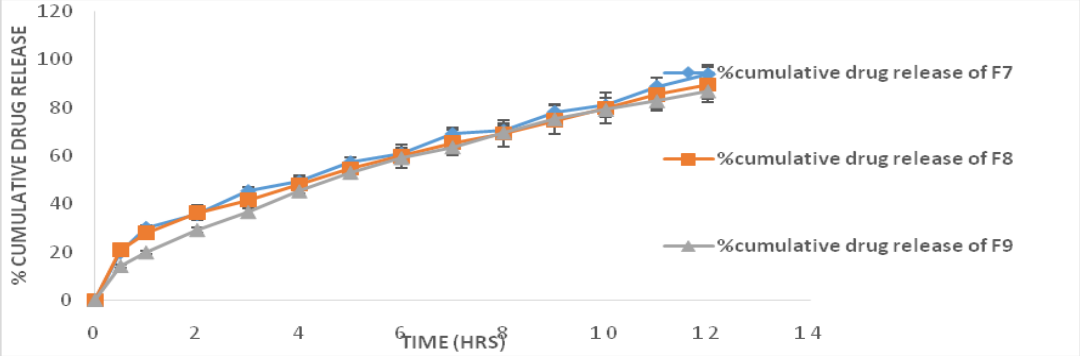

Fig.No.4: Dissolution profile of Esomeprazole floating tablets (F7, F8, F9 formulations)

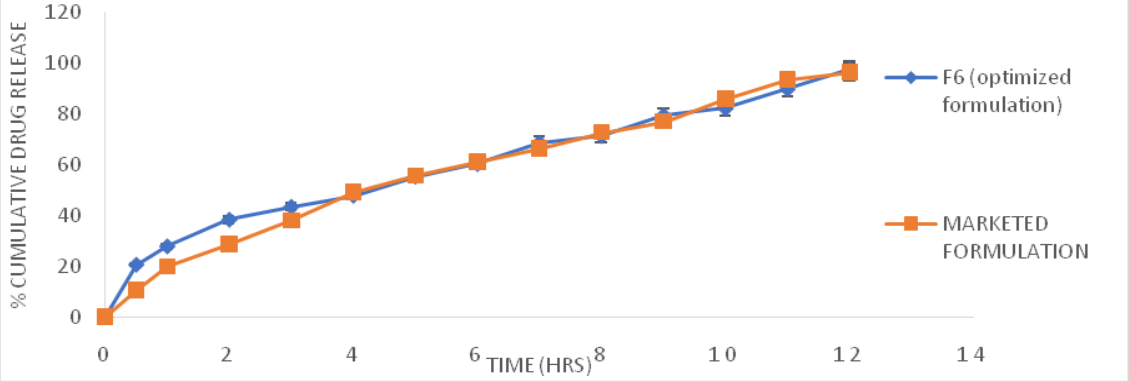

Fig.No.5: Dissolution profile of Esomeprazole Marketed formulation

Release Rate Kinetics to Dissolution Data

Various models were tested for explaining the kinetics of drug release. To analyze the mechanism of the drug release rate kinetics of the dosage form, the obtained data were fitted into zero-order, first order, Higuchi, and Koresmayer-Peppas release model.

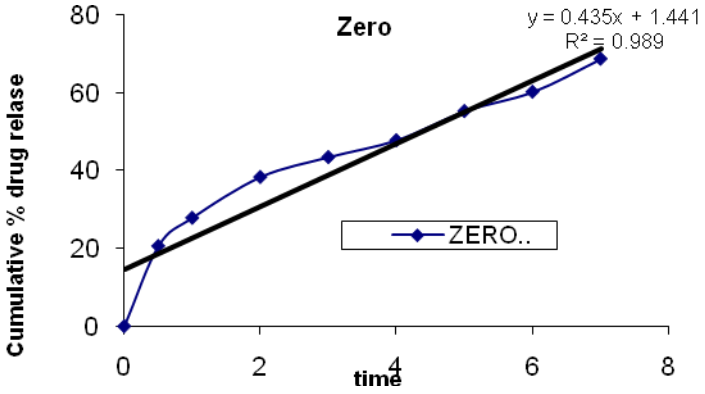

Fig.No.6: Zero order release kinetics graph

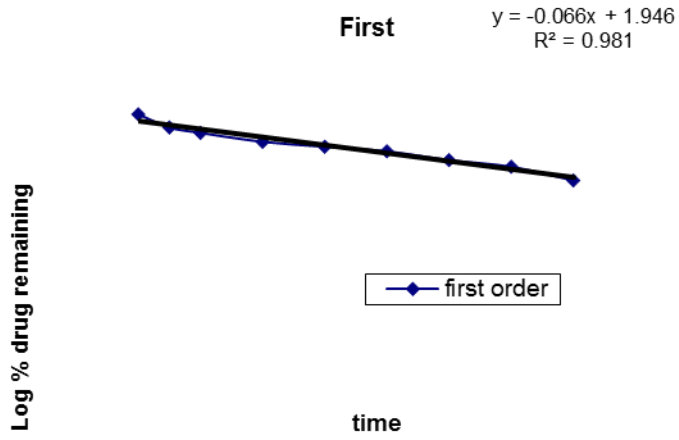

Fig.No.7: First order release kinetics graph

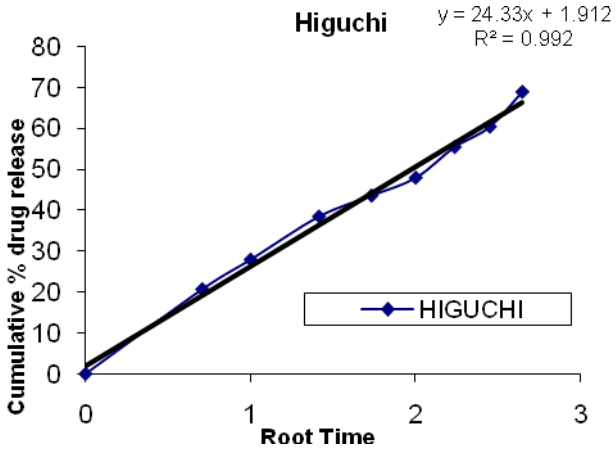

Fig.No.8: Higuchi release kinetics graph

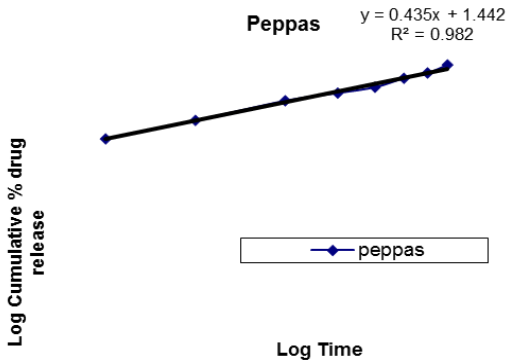

Fig.No.9: Kores mayer peppas graph

From the above graphs it was evident that the formulation F6 was followed zero order release kinetics.

Accelerated stability studies

The stability of optimized formulation was known by performing stability studies for three months at accelerated condition of 40^0C±75%RH on optimized formulation. The formulation was found to be stable,with no change in the weight variation, thickness, hardness, friability, floating lag time, drug content and *invitro* drug release pattern.

Table No.3: Accelerated stability studies of Optimized formulation(F6)

Parameters	**Temperature maintained: 40°C Relative humidity (RH): 75±5%RH**			
	Initial	**After 1 month**	**After 2 months**	**After 3 months**
Weight variation test(mm)	154.7±0.8	154.7±0.7	154.7±0.9	154.7±0.9
Thickness test (mm)	4.5±0.5	4.4±0.45	4.3±0.35	4.3±0.5
Hardness (Kg/cm^2)	4.2±0.2	4.2±0.3	4.1±0.2	4.1±0.4
Friability test (%)	0.45±0.4	0.45±0.3	0.45±0.2	0.45±0.2
Floating lag time	4.4±0.2	4.4±0.6	4.43±0.3	4.45±0.4
Drug content(%)	98.56±0.7	98.46±0.5	98.41±0.6	98.39±0.4
***In vitro* drug release (%)**	97.57±0.3	97.56±0.4	97.55±0.2	97.53±0.5

All the values are represented as Mean ± SD (n=3)

CONCLUSION

- Gastro retentive dosage form using HPMC K15M, chitosan, campritol ATO 888 was prepared to develop floating tablets of Esomeprazole that could retain in the stomach for longer period of time delivering the drug to the site of action i.e. stomach.
- Absorption maxima of Esomeprazole were determined based on the calibration curve. Calibration curve was developed by 0.1N HCL of pH 1.2.
- The formulation was developed by using different concentrations of Chitosan, Compritol 888 ato and HPMC K 15 M.
- The pre compression parameters of all formulations show good flow properties and these can be used for tablet manufacturing.
- The post compression parameters of all formulations were determined and the values were found to be satisfactory.
- From the drug content and *invitro* dissolution studies of the formulations, it was concluded that the formulation F6 shown best result i.e., the formulation prepared with HPMC K15 M, sodium bicarbonate, microcrystalline cellulose, magnesium stearate, talc retarded the drug release upto 12 hours in the concentration of 60mg of HPMC K15 M.
- From the accelerated stability studies, it was concluded that no change in the formulation

parameters which are performed at 40^0C±75%RH for three months.

As a result of this study it may be concluded that the floating tablets using HPMC K15 M in optimized concentration can be used to increase the GRT of the dissolution fluid in the stomach to deliver the drug in a controlled manner. The concept of formulating floating tablets of Esomeprazole offers a suitable and practical approach in serving desired objectives of gastro retentive floating tablets.

REFERENCES

[1]. Talukder R and Fassihi R. Gastroretentive Delivery Systems: A mini Review. Drug Development and Industrial Pharmacy 30(10), 2004, 1019-1028.

[2]. Hejazi R and Amiji N. Stomach specific anti H.Pylori therapy. I: Preparation and characterization of tetracycline of a floating multiple unit capsule, a high density loaded chitosan microspheres. Int. J.Pharm. 235, 2002, 87-94.

[3]. Cooerman M P, Krausgrill P, Hengels K J. Local gastric and serum amoxicillin concentration after different oral application forms. Antimicrob Agents Chemother 37, 1993, 150-615.

[4]. Ashok V Bhosale, Rahul V Takawale and sanjay D Sawamy. Oral novel drug delivery system. The Easterm pharmacist. 1, 2000, 41-43.

[5]. Brahmankar HA and Jaiswal SB. Biopharmaceutics and Pharmacokinetics A Treatise Vallabh Prakashan. Reprint Edition. 2, 2009, 348- 357 and 337.

[6]. Desai S. A Novel Floating Controlled Release Drug Delivery System Based on a Dried Gel Matrix Network Jamaica, NY, St John's University. 1, 1984, 1-25.

[7]. Vantrappen GR, Peeters TL, Janssens J. The secretory component of interdigestive migratory motor complex in man. Scand J Gastroenterol. 14, 1979, 663-667.

[8]. Wilson CG, Washington N. The stomach: its role in oral drug delivery. In: Rubinstein MH, ed. Physiological Pharmacetical: Biological Barriers to Drug Absorption. Chichester, UK: Ellis Horwood; 1, 1989, 47-70.

[9]. Kawashima Y, Niwa T, Takeuchi H, Hino T, Itoh Y. J Pharm Sci; 4, 1996, S182.

[10]. Rubinstein A, D R Friend. Specific delivery to the gastrointestinal tract. In Domb AJ (Ed) polymeric site-specific pharmacotherapy, wiley; Chichester; 1, 1994, 282-283.

[11]. Ritschel W A. Targeting in the gastrointestinal tract: new approaches, methods, Find Exp Clin Pharmacol, 13, 1991, 313-336.

[12]. Krogel I and Bodomeier R. Floating or pulsatile drug delivery systems based on coated effervescent cores. Int J Pharm; 187, 1999, 175-184.

[13]. Garg S, Sharma S. Gastroretentive drug delivery systems. Business briefing: Pharm Tech; 1, 2003, 160-166.

[14]. Khosla R, Feely L C, Davis S S. Gastrointestinal transit of non-disintegrating tablets in fed subjects. Int J Pharm; 53, 1989, 107-17.

[15]. Kutchai C H. The gastrointestinal system. In principal of physiology; MR Berna, M N Levy; Eds.; Mosby Year book;St. Louis MO, 2, 1996, 652-686.

[16]. Reddy S M, Sinha V R, Reddy D S. Novel and colonspecific drug delivery system for pharmacotherapy of peptide and non-peptide drugs. Drugs Today; 35(7), 1999, 537-580.

[17]. Mojaverian P, Vlasses P H, Kellner P E, Rocci M L. Effect of gender, posture and age on gastric residence time of an indigestible solid: Pharmaceutical considerations. Pharm Res; 5(10), 1998, 639-643.

[18]. Davis S S, Khosla R, Wilson C G, Washington N. The gastrointestinal transit of a controlled release pellet formulation of tiaprofemic acid. Int J Pharm; 33, 1987, 253-258.

[19]. Kinget R, Kalala W, Vervoort L, Mooter G V. Colonic drug targeting. J Drug Target; 6(2), 1998, 129-149.

[20]. Park H M, Cherish J M, Rosenback B D, Brunelle R L, Hargrove B, Wellman H N. Gastric emptying of enteric-coated tablets. Dig Dis Sci; 29, 1984, 207-212.