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Formulation and Evaluation of Floating Tablet of Omeprazole

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ABSTRACT:
In the current study a successful attempt was made to formulate bilayer floating tablets of clarithromycin and omeprazole by direct compression method containing loading dose, superdisintegrants in immediate release layer and maintenance dose, rate controlling polymers and gas generating agents in floating layer. The extended release was prepared by direct compression method using HPMC K15, HPMC K4, PVP K30, as sustained release polymer and sodium bicarbonate as gas generating agent to reduce floating lag time. Immediate release layer was prepared by direct compression using sodium starch glycolate, Croscarmellose sodium, crospovidone as super disintegrant. Gastro retentive floating drug delivery systems have been designed to increase its residence time in the stomach. The granules were evaluated for bulk density, tapped density, compressibility index, and Hauser's ratio.The granules showed satisfactory flow properties. The optimized tablets were compressed to obtain bilayer tablets. The tablets were evaluated for various physicochemical parameters and dissolution study. Further, the bilayer tablets were subjected to accelerated stability study. The omeprazole tablet showing more than 99.45 % release in 15 min and clarithromycin tablet showing more than 99.76 % release at the end of 12 h of initial lag time were compressed one above the other to obtain bilayer tablet. The similar release pattern was observed with the bilayer tablets as that of individual tablets. The bilayer tablets were found to be stable at the end of 6 months storage period as per ICH guidelines. Both the layers of the bilayer formulation showed desired drug release at the end of time period.

KEYWORDS: Floating Microspheres, Omeprazole, Solvent Evaporation Technique

I. INTRODUCTION:

The oral route is increasingly being used for the delivery of therapeutic agents because the low cost of the therapy and ease of administration lead to high levels of patient compliance. More than 50% of the drug delivery systems available in the market are oral drug delivery systems (Arora, 2005). The floating drug delivery system was first described by Davis (1968). Several approaches are currently used to prolong gastric retention time. These include floating drug delivery systems. FDDS are known as Hydro dynamically balanced systems or low-density system that has been made developed in order to increase the gastric transit time of drug. These microspheres are characteristically free flowing powders consisting of natural or synthetic polymers and ideally having a particle size less than 200μm. The goal of any drug delivery system is to provide a therapeutic amount of the drug to the proper site in the body to achieve promptly and then maintain the desired drug concentration [1]. Fixed dose combination therapy has various advantages over conventional monotherapy such as simpler dosage schedule leading to improved patient compliance and therefore improved treatment outcomes, reduced side effects and potentially lower cost of manufacturing, handling, packing and shipping compared to the costs of producing separate products [2]. The conventional dosage form produces wide fluctuation in drug concentration in the blood stream which led to the concept of sustained drug delivery. Gastro-retentive drug delivery is a novel approach of drug delivery which prolong the gastric emptying time. Many techniques such as floating drug delivery, low density, raft systems, mucoadhesive systems and high-density systems are under research. Floating drug delivery remains buoyant in the gastric content for a prolonged period of time. This improves bioavailability of drugs with narrow absorption window and poor solubility or stability in alkaline pH. Gastroesophageal reflux is the involuntary movement of gastric contents to the oesophagus. Gastroesophageal reflux is a normal physiological process that occurs several times a

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day without symptoms or damage of the oesophageal mucosa in most otherwise healthy individuals. Gastroesophageal reflux disease is a condition in which reflux of gastric contents into the oesophagus produces frequent or severe symptoms that negatively affect the individual's quality of life or result in damage to oesophagus, pharynx, or the respiratory. To retain the drug in the stomach and for drugs with poor solubility and low stability in intestinal fluids floating drug delivery systems (FDDS) are invented. The concept behind the Floating Drug Delivery System is making the dosage form less dense than the gastric fluids to make it float on them2. They stay buoyant in the stomach for a long time without affecting the gastric emptying rate for a prolonged period, with the potential for constant release of drugs. While the system is floating on the gastric content, the drug is slowly released from the system at the desired rate. After the drug has been released, the residual system is emptied from the stomach3. FDDS or Hydro-dynamically balanced systems (HBS) are low-density systems having the sufficient tendency to float over the gastric contents and remain in the stomach for an extended period that releases the drug component at the desired rate while floating over the gastric contents it contributes to increased gastro retention time and reduced fluctuation. FDDS is the mechanism of a gastro-retentive drug delivery system that controls the pharmacokinetic release of a drug to a specific site to achieve its pharmacological action. Controlled gastric retention of solid dosage form may be realized by the mechanism of mucoadhesion, floatation, sedimentation, expansion, modified shape system or by simultaneous administration of pharmacological agents which delay gastric emptying. Scintigraphic studies determining gastric emptying rates elucidated that orally administered controlled release dosage forms are was subjected to complications.

I. Short gastric residence time.
II. Unpredictable gastric emptying rate [1].

OBJECTIVE:

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. It is also reported that oral treatment of gastric disorders with an H2-receptor antagonist like Omeprazole used in combination with antacids promotes local delivery of these drugs to the receptor of the parietal cell wall. Local delivery also increases the stomach wall receptor site bioavailability and increases the drugs' ability to reduce acid secretion [2].

MATERIALS AND METHODS:

Hydroxypropyl methyl cellulose (HPMC K15, HPMC K4), Polyplasdone XL (Crospovidone) and Glycols (sodium starch glycolate) were generously gifted by Colorcon Asia Pvt.Ltd. (Goa, India), International Specialty Product Ltd. (Mumbai, India) and Roquette India Pvt.Ltd. (Mumbai, India) respectively. Ac-Di-Sol (Croscarmellose sodium) and (Microcrystalline cellulose) were supplied by Signet Chemical Corporation Pvt. Ltd. (Mumbai, India). Talc, lactose, citric acid, NaHCO3, was purchased from Loba Chemie Pvt.Ltd. (Mumbai, India). All other chemicals and reagents were of analytical grade.

METHODS:

Esomeprazole magnesium trihydrate was gifted by Aurobindo pharma limited, A.P, India. Crospovidone, Sodium starch glycolate, Croscarmellose sodium obtained from Danmed Pharmaceuticals Pvt Ltd, Hyderabad. Lactose DC and Mannitol DC were procured from SD Fine Chemicals Limited, Mumbai. Acryl EZE (Eudragit L 30 D55, Colorcon) was supplied by Med Reich Limited, Bangalore. Polypropylene, Calcium silicate, Aerosol purchased for from Sigma Aldrich, Bangalore. Xanthan gum, Guar gum, HPMC K4M, MCC was purchased from INR Chem and yarrow chemicals, Mumbai. Omeprazole magnesium was kindly provided by Dr Reddy's Laboratories, Hyderabad, sodium carbonate sodium alginate, methyl paraben, and propyl paraben were procured from Arora and company, Delhi, Sodium citrate and Hydrochloric Acid form Central Drug House (P) Ltd., New Delhi, Calcium chloride from Loba Chemicals, Mumbai. All chemical and reagents used were of analytical grade. De-ionized water was used for the complete study.

➢ **Preformulation studies:**

Preformulation studies required to ensure the development of a stable as well as therapeutically effective and safe dosage form. These studies focus on the physicochemical properties of the drug that could affect performance and development of an efficacious dosage form.

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➢ **Description of drug:**

Organoleptic properties of drug, that is, colour, odour, and taste were observed.

➢ **Identification of drug:**

UV spectrophotometric analysis of drug Ultraviolet absorption in the range 200–400 nm of a 100 µg/ml solution of the drug in 0.1 N HCl was determined.

➢ **Analytical estimation of drug:**

The standard stock solution of omeprazole magnesium was prepared by dissolving 10 mg of drug in 0.1N HCl in 100 ml volumetric flask. Stock solution of omeprazole magnesium was further diluted in 0.1 N HCl to get standard solution of 100 µg/ ml. The resulting solution was then scanned between 200 and 400 nm UV visible spectrophotometer [3].

Preparation of omeprazole floating microspheres:

The floating micro spheres were prepared by solvent evaporation method. 0.75g of polyvinyl alcohol was dissolved in 100 ml of distilled water. Different quantities of Ethyl cellulose and Eudragit S 100 were dissolved in dichloromethane by magnetic stirrer. A known quantity of Omeprazole was dissolved in above polymer solution along with surfactant (span 80). The resulting solution was added drop wise into the aqueous phase containing polyvinyl alcohol with continuous stirring at 700 rpm using mechanical stirrer. The microspheres were prepared by solvent evaporation method.0.46g of polyvinyl alcohol is dissolved in 100ml of distilled water. Different quantities of Ethyl cellulose, HPMC and Eudragit RS100 in individual and combination of these polymers was dissolved in dichloromethane by using magnetic stirrer. A known quantity of Omeprazole (40mg) was dissolved in the above polymeric solution along with 0.1% of polyethylene glycol (surfactant). The resulting solution was then poured into 500ml beaker, containing 150ml of polyvinyl alcohol (0.46%w/v).

Characterization of microspheres:

The prepared floating microspheres were evaluated for product yield, drug content, entrapment efficiency and drug release studies. Buoyancy time and percentage of buoyancy was determined. Process parameters such as stirring time, stirring speed and organic to aqueous phase ratio were optimized. Floating microspheres were prepared at 1:2, 1:5 and 1:10 organic to aqueous phase ratio. There was no formation of microspheres at 1:2 organic to aqueous phase ratio. Microsphere formation was observed at 1:5 and 1:10 organic to aqueous phase ratio. Total five formulations were prepared by altering drug to polymer ratio to study the effect of polymer concentration upon evaluation parameters such as product yield, drug content, entrapment efficiency, in vitro drug release and percentage of buoyancy. 1) Percentage Yield The dried floating microspheres of Omeprazole were weighed and percentage yield of the prepared microspheres was calculated by using the following formula (Prakash et al., 2007). Percentage yield = {the weight of microspheres / the weight of polymer + drug}*100 2) Drug Content The various batches of the dried floating microspheres of Omeprazole microspheres were subjected for drug content analysis[4].

EVALUATION OF OMEPRAZOLE MICROSPHERES:

Bulk density and tapped density:

Bulk density and tapped density were measured by using 10ml graduated cylinder. The sample poured in the cylinder was tapped mechanically for 100 times, then tapped volume was noted and bulk density and tapped density were calculated.

Each experiment for micromeritic properties was performed in triplicate manner.

Bulk density = Mass / Volume

Tapped density = Mass / Tapped volume

Carr's index:

Compressibility index is an important measure that can be obtained from the bulk and tapped densities. According to the theory, the less compressible material is more flow able. A material having values less than 20 to 30% is defined as the free flowing material, based on the apparent bulk density and tapped density, the percentage compressibility of the bulk drug was determined by using the following formula. It is expressed in percentage and is expressed by

I = Dt - Db / Dt x 100

Where, **Dt** is the tapped density of the powder and Db is the bulk density of the powder.

Hausner's ratio:

It indicates the flow properties of the powder and the ratio of Tapped density to bulk density of the powder or granules is called Hausner"s ratio.It is expressed in percentage and is expressed by

H= Dt / Db

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Where, Dt is the tapped density of the powder and Db is the bulk density of the powder.

Angle of repose:

Angle of repose of different formulations was measured by fixed funnel standing method. Microspheres were weighed and passed through the funnel, which was kept at a certain height from horizontal surface. The passed microspheres formed a pile of height „h" above the horizontal surface and the pile was measured. The angle of repose was determined by

Angle of repose (θ) = Tan-1 (h / r)

Where, h is the height of pile and r is radius.

Percentage yield:

Dried microspheres were accurately weighed and the percentage yield4 was calculated by

% yield = (Practical yield/Theoretical yield) × 100

IN VITRO BUOYANCY STUDIES:

The microspheres weighed about 0.3g were taken in the USP dissolution apparatus II which was filled with 900ml of phosphate buffer containing 0.02% of tween20. The medium was agitated with paddle rotating at 100 rpm for 12hrs.The floating and settled portions were taken separately dried and weighed. Buoyancy percentage was calculated by using the formula (Sunil, 2014) % Buoyancy = weight of floating microspheres/initial weight of microspheres ×100

Invitro Drug Release Study of Microsphere Formulations in Phosphate Buffer p H 7.2 The dissolution rate testing apparatus was employed to study the release of omeprazole floating using phosphate buffer pH 1.2 as a dissolution medium. 50mg equivalent of omeprazole containing ethyl cellulose microspheres was taken and dissolution test was being carried out at 50rpm maintained at 370 c + 0.50 c. 5ml of sample were withdrawn at specific time interval for 24 hours. The sample volume was replaced by an equal volume of fresh medium. The concentration was determined spectrophotometrically atthe same procedure was repeated for other formulations also[5].

TYPES OF FLOATING DRUG DELIVERY SYSTEM:

The systems that are developed to increase the gastric residence time of oral dosage forms are as follows:

- Non-effervescent system
- Effervescent system

Non- effervescent:

The Non-effervescent FDDS is based on the mechanism of swelling of polymer or adhesion to the mucosal layer in the GI tract. The most commonly used excipients in non-effervescent FDDS are gel-forming or highly swellable cellulose-type hydrocolloids, hydrophilic gums, polysaccharides, and matrix-forming materials such as polycarbonate, polyacrylate, polymethacrylate, polystyrene as well as bio adhesive polymers such as Chitosan and carbopol. The formulation method includes a simple approach of thoroughly mixing the drug and the gel-forming hydrocolloid. After oral administration, this dosage form swells in contact with gastric fluids and attains a bulk density of < 1. The air entrapped within the swollen matrix imparts buoyancy to the dosage form. The so-formed swollen gel-like structure acts as a reservoir and allows sustained release of the drug through the gelatinous mass.

The various types of this system are as follows:

- Colloidal gel barrier systems / Single Layer Floating Tablets
- Bi-layer f l o a t i n g tablets
- Microporous compartment systems
- Multi-particulate system: Floating Beads / Alginate Beads
- Micro balloons / Hollow Microspheres

Effervescent system:

These are matrix types of systems prepared with the help of swellable polymers such as methylcellulose and chitosan and various effervescent compounds, e.g., sodium bicarbonate, tartaric acid, and citric acid. They are formulated in such a way that when in contact with the acidic gastric contents, CO2 is liberated and gas entrapped in swollen hydrocolloids which provides buoyancy to the dosage forms. The various types of this system are:

- Volatile liquid-containing systems
- Gas generating systems[6]

GASTRO RENTENTIVE DRUG DELIVERY SYSTEMS (GRDDS)

Floating systems:

The formulation is able to float in the gastric fluid due to the low density of floating systems, where it may stay for a longer period of time without changing the pace at which the stomach empties. The low density is due to the swelling of polymer and gas generation. Polymer-based systems expand in the presence of gastric fluid and float in the juice. The low-density gas

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generating system works by the production of carbon dioxide when it comes in contact with gastric fluids. This system is suitable for H. pylori bacteria due to its localized action, which will directly deliver antibiotics in the gastric mucosa for longer periods. According to Javadzadeh et.,al. the floating system is suitable for medications that act locally on the stomach's gastric mucosa, such as metronidazole. Using this system, antimicrobial drugs can be applied topically to cure H. pylori infection, which may be helpful to prevent the adverse effects of traditional triple therapy. The floating microspheres of clarithromycin developed by Tejaswi et al., to eradicate H. pylori bacteria showed 71% entrapment efficiency of the drug, and 82% of the microsphere floated for more than 12 h (11). Patel et al. and Emara et al., reported that the floating tablet of clarithromycin and amoxicillin has improved the prolonged release of the drug to the intestinal mucosa.

Muchoadhesive systems:

Bio adhesive polymers are used in this method so that they may stick to the stomach epithelial lining. Hydrophilic gelling chemicals coupled with several hydrogen-bond forming groups, such as sulphate, carboxyl, amide, and hydroxyl groups, are characteristic of macromolecular bio adhesive polymers. These include polycarbophil, carbopol, lectins, chitosan and gliadin etc. Villegas et al. developed a mucoadhesive system (mucolast) to eradicate H. pylori infection using amoxicillin and clarithromycin. Pharmacokinetics evaluation of the formulation showed more drug concentration on the stomach lining than in the systemic circulation. In-vivo efficiency of mucolast was done in H. pylori infected mice and showed significant results in terms of histopathological findings [136]. Dey et al. prepared floating mucoadhesive beads of amoxicillin trihydrate. The developed beads imparted good floating behaviour for more than 24 h having a floating lag time of 46.3 ± 3.2 s. The optimized batch completely inhibited H. pylori development in in vitro culture after 15 h. A floating and mucoadhesive system combination showed good in vitro results and localized action. Drug release from these beads was maintained via a mucin layer that was not disturbed, replicating the in vivo circumstances in which H. pylori is found in the gastric lining.

High density systems:

The density of the system is an essential feature for the stomach retention of the formulation. A high-density system uses its weight for the retention mechanism. When the system's density is higher than the gastric fluid, it will automatically descend to the stomach's bottom, placed below the pylorus. As a result of their resistance to the peristaltic contraction of the gastric wall, they eventually become imprisoned in the antrum. As a result, this system's stomach residency time is greatly extended. Commonly used density enhancers are iron, titanium dioxide, barium sulphate, zinc oxide powder, etc., increasing density by up to 1.5–2.4 g/m.

Magnetic systems:

In this system, a dosage form is made of excipients, internal magnets, and active medicinal components. To control the location of the magnetic field, an extracorporeal magnet is placed over the stomach. The intensity produced by the extracorporeal magnet can affect gastro retention [146]. Some studies reported that the magnetic system increases the gastroprotection and bioavailability of the formulation [147,148]. This system has some drawbacks, like difficulty in precise positioning of the magnet and can result in low patient compliance. Silva-Freitas et al. developed magnetic polymeric stimulus-responsive particles for antimicrobial therapy in the stomach. The final composition of the microparticles was 9.0 ± 0.3% magnetite, 87.0 ± 2.3% Eudragit and 4.3 ± 1.5% amoxicillin. The optimized microparticles had a size of 17.2± 0.4 µm.

Expandable system:

This system is designed to have a longer gastro retention time by increasing their volume or shape. To function properly, an expandable system must meet three criteria: it must be small enough to be taken orally, in order to avoid passing through the pyloric sphincter, it must expand only in the stomach, and it must contract again after drug release is complete so that it can be expelled. This formulation is also termed a "plug-type" system because it can block the pyloric sphincter. The system development occurs by the two methods, swelling and unfolding, allowing volume and shape modification. Yang et al. fabricated a swellable asymmetric triple-layer tablet containing tetracycline, metronidazole, and bismuth for treating H. pylori that uses a floating feature to increase the retention period of drug in stomach[7].

ADVANTAGES:

- FDDS is advantageous for drugs meant for local action in the stomach eg: Antacids

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- The FDDS is advantageous for drugs absorbed through the stomach eg: Ferrous salts, Antacids
- A floating dosage form is a widely accepted approach, especially for drugs that have limited absorption sites in the upper small intestine
- FDDS dosage forms are advantageous in cases of vigorous intestinal movement and in diarrhea to keep the drug in a floating condition in the stomach to get a relatively better response.
- Acidic substance like aspirin irritates the stomach wall when come in contact with it hence; HBS/FDDS formulations may be useful for the administration of aspirin and other similar drugs.
- Ease of administration and case compliance.
- Reduces the frequence of dosing.
- It enhances the bioavailability of drugs.
- The active ingredient is administered directly to the site of action, which reduces or eliminates adverse effects.

DISADVANTAGES:

- Many factors impact stomach retention, comprising gastric motility, pH, and the existence of food. Because these variables are never consistent, buoyancy cannot be anticipated.
- Drugs that irritate or cause damage to the stomach mucosa should not be designed as floating drug delivery devices.
- Due to its all-or-none-emptying procedure, there is a lot of difference in stomach emptying time.
- Patients should not be given floating types right before bedtime.
- For drugs with a problem [challenge, difficulty] of solubility (or) uniformity in stomach fluids, a floating system is not an option [8].

TREATMENT:

Proton pump inhibitors:

All currently approved PPIs are benzimidazole derivatives: heterocyclic organic molecules that include both a pyridine and benzimidazole moiety linked by a methylsulfonyl group. The prototypical example of this structure, Omeprazole, was the first clinically useful PPI. Subsequently introduced drugs include Lansoprazole, Pantoprazole, Rabeprazole, and the stereo-isomeric compounds Esomeprazole and Dexlansoprazole. Although each of these drugs has different substitutions on their pyridine and/or benzimidazole rings, in general, they are remarkably similar in their pharmacological properties.

Mechanism of action:

PPI mechanism of action is characterized mainly by irreversible inhibition of the enzyme system called Hydrogen/Potassium adenosine triphosphate (H+/K+ATPase), this enzyme system which is located in the gastric parietal cells acts by promoting continuous proton release into the gastric lumen, this action of H+/K+ ATPase system is the reason behind its popular name as the proton pump, the proton pumping is regarded as the final stage of the stomach acid production and inhibition of this process will provide a powerful reduction in the gastric acid content. The PPIs are administered as prodrugs, which means in their inactive form, they need to be activated before exerting their full action. The activation process of PPIs requires a protonation step of the tertiary amines in the drug structure before the rearrangement step which provides the active form of the compound[9].

Table-1: The category of drugs and its mechanism of action and adverse effects

Category	Drug	Mechanism of action	Adverse effects
Proton pump inhibitors	Omeprazole, lansoprazole, rabeprazole, pantoprazole	Inhibition of the gastric H+/K+ ATPase (proton pump) enzyme system	Headache, abdominal pain, diarrhoea, nausea, vomiting, constipation, flatulence, Vit B12 deficiency, osteoporosis
H2receptors blockers	Cimetidine, Famotidine, Nizatidine, Ranitidine	Blocking the action of histamine at the histamineH2 receptors of perital cells	Headache, anxiety, depression, dizziness, cardiovascular events, thrombocytopenia
antacids	Aluminium hydroxide,	Increases gastric pH to greater than four, and	Frequency not defined: Nausea, vomiting,

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	Magnesium hydroxide	inhibits the proteolytic activity of pepsin Causes osmotic retention of fluid.	constipation, abdominal cramping, diarrhea, electrolyte imbalance.
Potassium	vonoprazan	Inhibits H+, K+ ATPase in gastric.	Nasopharyngitis, fall, confusion.

II. RESULTS AND DISCUSSION:

The melting point of clarithromycin and omeprazole was 220- 221ºC and 155-157 ºC respectively.The UV absorption of 10µg/ml for clarithromycin (react with methyl orange and extract with chloroform) and omeprazole in 0.1N HCL in the range of 200-800 nm exhibit maximum at 306 nm in case of omeprazole and at 416 nm in case of clarithromycin using U.V.Results of Omeprazole Floating Microspheres Formulated at 1:5 Organic to Aqueous Phase Ratio the prepared five formulations of 1:5 organic to aqueous phase ratio were evaluated for product yield.Different formulation of omeprazole microspheres at 1:5 organic at aqueous phase ratio.

Table-2: omeprazole floating microspheres at 1:5 organic at aqueous phase ratio

Code	ratio	Practical yeild	Drug content	Entrapment efficacy	% drug release	%Buoyancy
F1	1:15	75.9%	50%	94.1%	67.2%	74.8%
F2	1:20	78.5%	52.8%	94.3%	66%	76.1%
F3	1:25	80.1%	53.8%	87.5%	63.2%	70.9%
F4	1:30	79.1%	53.3%	93.2%	58.4%	76.3%
F5	1:35	86.4%	93.9%	98%	62.9%	72.8%

Invitro drug release:

Different Formulations of Omeprazole Microspheres at 1:5 Organic to Aqueous Phase Ratio: In vitro data of prepared Omeprazole magnesium loaded with ethyl cellulose microspheres at 1:5 organic to aqueous phase ratio

Table-3: Invitro data of prepared omeprazole floating microspheres at 1:5 organic to aqueous phase ratio

Time	F1	F2	F3	F4	F5
30mins	5.5%	4.2%	9.5%	5.3%	4.5%
1hr	8.4%	8.4%	18.2%	6%	7.2%
2hr	11.9%	12.6%	20%	8.4%	12.3%
3hr	14.1%	14.2%	24.3%	13.2%	14.5%
4hr	17.9%	18.3%	26.4%	14.1%	17.2%
5hr	21.6%	19.9%	28.5%	16.6%	18.9%
6hr	26.5%	22.5%	31.7%	18.9%	21.5%
7hr	30.6%	25%	35%	21.5%	32.1%
8hr	33.2%	27.3%	39.6%	24%	37.6%
9hr	38.4%	32.3%	42.2%	27.1%	39.9%
10hrs	40.7%	39.4%	44%	27.8%	48.2%
11hrs	51%	42.5%	48%	32.5%	49%
12hrs	67.2%	66%	63.2%	58.4%	62.9%

- The micromeritic properties such as of bulk density, tapped density, angle of repose, compressibility index, Hausner's ratio and particle size distribution of omeprazole instant release layer blend and clarithromycin gastro retentive layer were studied. The all the blends/ granules have shown good compression properties. The value of bulk density indicates good packing characteristics.
- Treatment of peptic or gastric ulcer requires an antibacterial agent like clarithromycin, a broad-spectrum antibacterial agent, which is effective against peptic ulcer causing h. pylori bacteria and a gastric acid suppressing drug

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like esomeprazole magnesium trihydrate, a proton pump inhibitor.

- has its absorption window in stomach where as esomeprazole is absorbed well from small intestine because of its instability in stomach. In lieu of the previous reports, in the current investigation a novel core in coat gastro retentive tablets were developed by compression coating method.
- The dosage form containing 20 mg of esomeprazole presented as enteric coated core tablet within coat formulation containing 250 mg clarithromycin dispensed as a single unit. Further the clarithromycin coat tablets were formulated as FDDS or GRDF and esomeprazole core as enteric release tablets[10].

DISCUSSION:

In the present investigation Omeprazole loaded Floating microspheres were prepared by solvent evaporation technique. Process parameters such as stirring time, stirring speed and organic to aqueous phase ratio were optimized. Floating microspheres were prepared at 1:2, 1:5 and 1:10 organic to aqueous phase ratio. There was no formation of microspheres at 1:2 organic to aqueous phase ratio. Microsphere formation was observed at 1:5 and 1:10 organic to aqueous phase ratio. Total five formulations were prepared at each 1:5 and 1:10 organic to aqueous phase ratio by altering drug to polymer ratio to study the effect of polymer concentration upon evaluation parameters such as product yield, drug content, entrapment efficiency, in vitro drug release and percentage of buoyancy. Out of five formulations prepared at 1:5 organic to aqueous phase ratio On F5 formulation was concluded as the best formulation because of highest product yield, more drug content, Highest entrapment efficiency and sustained drug release properties. The percentage of buoyancy was found to be 72.8% for F5 formulation. In vitro drug release profiles of both the formulations were compared. On comparison from F5 formulation prepared at 1:5 organic to aqueous phase ratio 68.9% of drug was released in a time period of 12 hours proving its sustain release property. Several plots were drawn for F5 formulation to determine the order of kinetics and mode of drug release. From the plots it was concluded that the formulation follows zero order kinetics with fickian diffusion mechanism.

III. CONCLUSION:

The optimised Bilayer tablet of clarithromycin and omeprazole was formulated and evaluated for various evaluation parameters i.e. Hardness-5.13 kg/cm2. Friability 0.82%, Thickness 5.42 mm and floating time of 12hrs. All the results of evaluations were found to be within limits and the final Optimised bilayer formulation released 98.23 % in 12hrs.Thus the optimised Bilayer floating tablets of clarithromycin and omeprazole appears suitable for further pharmacodynamic and pharmacokinetic studies to evaluate the clinical safety of these Bi-layered Floating tablets in suitable animals and human models. Finally, it may be concluded that this novel drug delivery system that is Bi-layered Floating Tablet offers a valuable dosage form which delivers the drug at a controlled rate and at a specific site. Over the years, attempts have been made to control the time course and specificity of the drug in the body through a verity of drug modifications and dosage forms. The need of making any drug microspheres is to produce a drug delivery system which is safe and capable of producing consistent therapeutic blood levels of drug in the body for required period of time. It is also improves keeping and handling properties of the drug. The study conclusively demonstrated a floating tablet of Omeprazole, prepared using mixture of HPMC K15M and HPMC K100M as polymer, were successfully be prepared by wet granulation method which will lead to improved patient compliance and product quality. The technique adopted for the preparation of floating tablet was wet granulation. A comparative Omeprazole release study from pure drug and optimum batch in 0.IN HCL pH 1.2 was performed.

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