WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 10, Issue 4, 1917-1971. Research Article ISSN 2277– 7105

PREPARATION AND EVALUTION OF GASTRORETENTIVE FLOATING TABLETSOF LANSOPRAZOLE

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Article Received on
21 Feb. 2021,

Revised on 13 March 2021,
Accepted on 02 April 2021

DOI: 10.20959/wjpr20214-20231

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ABSTRACT

The purpose of the present study was to develop a gastric floating tablets of Lansoprazole were prepared by direct compression method of 120 mg of Lansoprazole. Floating tablet of Lansoprazole increases the gastric residence time as well as bioavailability and there by showed increased therapeutic efficacy. The addition of gel forming polymers and gas generating agent sodium bicarbonate and citric acid was essential to achieve *in vitro* buoyancy. In FTIR studies Lansoprazole are also present in the physical mixture, which indicates that there is no interaction between drug and the polymers, which confirms the stability of the drug. Pre formulation studies were conducted to select suitable excipient. Combination of different excipient was used to formulate Lansoprazole floating tablets. The evaluation parameter such as weight variation, thickness, Hardness, Friability, *In vitro* drug release studies was conducted. The results were with in the limit and compared with marketed formulation. From the results obtained, Formulation F6 gives desirable Sustained effect for 12 hours having 99.81 % drug release at the end of the 12 hours. formulation F6 contain Guar gum in concentration 45 mg. Release model of sample was found to follow Kors mayer peppas release kinetics with high linearity.

KEYWORDS: Lansoprazole, Xanthan gum, Guar gum, Sodium Alginate and Floating Tablets.

1. INTRODUCTION

Oral delivery of drugs is the most preferable route of drug delivery. Oral route is considered most natural, uncomplicated, convenient and safe due to its ease of administration, patient compliance and flexibility in formulation and cost effective manufacturing process.[1] Many of the drug delivery systems, available in the market are oral drug delivery type systems

Pharmaceutical products designed for oral delivery are mainly immediate release type or conventional drug delivery systems, which are designed for immediate release of drug for rapid absorption.

These immediate release dosage forms have some limitations such as.

1. Drugs with short half-life require frequent administration, which increases chances of missingdose of drug leading to poor patient compliance.
2. A typical peak-valley plasma concentration-time profile is obtained which makes attainmentof steady state condition difficult.
3. The unavoidable fluctuations in the drug concentration may lead to under medication orovermedication as the Css values fall or rise beyond the therapeutic range.
4. The fluctuating drug levels may lead to precipitation of adverse effects especially of a drugwith small therapeutic index, whenever overmedication occurs.[2]

In order to overcome the drawbacks of conventional drug delivery systems, several technical advancements have led to the development of controlled drug delivery system that could revolutionize method of medication and provide a number of therapeutic benefits.[3]

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 systems4. Controlled-release drug delivery systems (CRDDS) provide drug release at a predetermined, predictable, and controlled rate. Controlled-release drug delivery system is capable of achieving the benefits like maintenance of optimum therapeutic drug concentration in blood with predictable and reproducible release rates for extended time period; enhance ment of activity of duration for short half-life drugs; elimination of side effects; reducing frequency of dosing and wastage of drugs; optimized therapy and better patient compliances.[5,6]

The successful development of oral controlled drug delivery systems requires an understanding of the three aspects of the system, namely.

1. The physiochemical characteristics of the drug.
2. Anatomy and physiology of GIT and Characteristics of Dosage forms.[4]

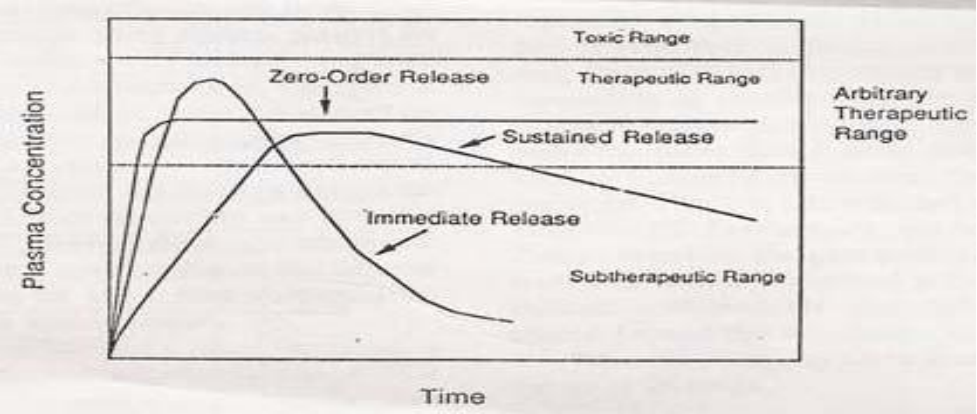


Fig 1.1: Drug level verses time profile showing differences between zero order, controlled releases, slow first order sustained release and release from conventional tablet.

Oral drug delivery systems have progressed from immediate release to site-specific delivery over a period of time. Every patient would always like to have a ideal drug delivery system possessing the two main properties that are single dose or less frequent dosing for the whole duration of treatment and the dosage form must release active drug directly at the site of action.[7]

Thus the objective of the pharmacist is to develop systems that can be as ideal system as possible. Attempts to develop a single- dose therapy for the whole duration of treatment have focused attention on controlled or sustained release drug delivery systems. Attention has been focused particularly on orally administered sustained drug delivery systems because of the ease of the administration via the oral route as well as the ease and economy of manufacture of oral dosage forms. Sustained release describes the delivery of drug from the dosage forms over an extended period of time. It also implies delayed therapeutic action and sustained duration of therapeutic effect. Sustained release means not only prolonged duration of drug delivery and prolonged release, but also implies predictability and reproducibility of drug release kinetics. A number of different oral sustained drug delivery systems are based on different modes of operation and have been variously named, for example, as dissolution controlled systems, diffusion controlled systems, ion-exchange resins, osomotically controlled systems, erodible matrix systems, pH- independent formulations, swelling controlled systems, and the like.

An orally administered controlled drug delivery system encounters a wide range of highly variable conditions, such as pH, agitation intensity, and composition of the gastrointestinal

fluids as it passes down the G.I tract. Considerable efforts have been made to design oral controlled drug delivery systems that produce more predictable and increased bioavailability of drugs. However, the development process is precluded by several physiological difficulties, like inability to retain and localize the drug delivery system within desired regions of the G.I tract and highly variable nature of the gastric emptying process. An important factor, which may adversely affect the performance of an oral controlled drug delivery system, is the G.I transit time. The time for absorption in the G.I transit in humans, estimated to be 8-10 hr from mouth to colon, is relatively brief with considerable fluctuation. G.I transit times vary widely between individuals, and depend up on the physical properties of the object ingested and the physiologicalconditions of the gut. This variability may lead to predictable bioavaialability and times to achieve peak plasma levels. One of the important determinants of G.I transit is the residence timein the stomach.

Majority of the drugs are well absorbed from all the regions of the G.I tract while some are absorbed only from specific areas, principally due to their low permeability or solubility in the intestinal tract, their chemical instability, the binding of the drug to the gut contents, as well as to the degradation of the drug by the microorganisms present in the colon. Therefore, in instances where the drug is not absorbed uniformly over the G.I tract, the rate of drug absorption may not be constant in spite of the drug delivery system delivering the drugs at a constant rate into the G.I fluids. More particularly, in instances where a drug has a clear cut absorption window, i.e., the drug is absorbed only from specific regions of the stomach or upper parts of thesmall intestine; it may not be completely absorbed when administered in the form of a typical oral controlled drug delivery system. It is due to the relatively brief gastric emptying in humans, which normally averages 2-3 hrs through the major absorption zone. It may cause incomplete drug release from the dosage form at absorption sites leading to diminished efficacy of the administered dose. It is apparent that for a drug having such an absorption window, an effective oral controlled drug delivery system should be designed not only to deliver the drug at acontrolled rate, but also to retain the drug in the stomach for a long period of time. For this drug, increased or more predictable availability would result if controlled release systems could be retained in the stomach for extended periods of time.

It is suggested that compounding narrow absorption window drugs in a unique pharmaceutical dosage form with gastro retentive properties would enable an extended absorption phase of these drugs. After oral administration, such a dosage form would be

retained in the stomach and release the drug there in a controlled and prolonged manner, so that the drug could be supplied continuously to its absorption sites in the upper gastrointestinal tract. This mode of administration would best achieve the known pharmacokinetic and pharmacodynamic advantages of controlled release dosage form for these drugs.[7]

Gastrointestinal retention

Gastro retentive systems can remain in the gastric region for several hours and hence significantly prolong the gastric residence time ofdrugs. Prolonged gastric retention improves bioavailability, reduces drug waste, and improves solubility for drugs that are less soluble in aigh pH environment. It has applications also for local drug delivery to the stomach and proxima small intestines. Gastro retention helps to provide better availability of new products with new therapeutic possibilities and substantial benefits for patients5. To successfully modulate the gastrointestinal transit time of a drug delivery system through floating drug delivery system (FDDS) For maximal gastrointestinal absorption of drugs and site-specific delivery, on needs to have a good fundamental understanding ofthe anatomic and physiological characteristics of the human GIT. These are outlined and briefly discussed1.

Stomach anatomy[8,9,10]

The main function of the stomach is to process and transport food. It serves as a short-term storage reservoir, allowing a rather large meal to be consumed quickly. Substantial enzyme tic digestion isinitiated in stomach, particularly of proteins. Vigorous contractions of gastric smooth muscle mix and grind foodstuffs with gastric secretions, resulting inliquefaction of food. As food is liquefied in the stomach, it is slowly released into the small intestine for further processing6.Anatomically the stomach is divided into 3 regions: fundus, body, and antrum (pylorus). The proximal part made of fundus and body acts as a reservoir for undigested material, whereas the antrum is the main site for mixing motions and act as a pump for gastric emptying by propelling actions.[7] It has been reported that the mean valueof pH in fasted healthy subjects is 1.1± 0.15. But when food comes into the stomach, the pH may rise to levels in the 3.0 to 4.0 level due to the buffering capacity of proteins. However, in fasted state, basal gastric secretion in women is slightly lower than that of men.[8] Gastric emptying occurs during fasting as well as fed states. The pattern of motility is however distinct in the 2 states. During the fasting state an interdigestive series of

electrical events take place, which cycle both through stomach and intestine every 2 to 3 hours. This is called the interdigestive myloelectric cycle or migrating myloelectric cycle (MMC), which is further divided into following 4 phases.

1. Phase I (Basal phase) lasts from 30 to 60 minutes with rare contractions.
2. Phase II (Preburst phase) lasts for 20 to 40 minutes with intermittent action potential and contractions. As the phase progresses the intensity and frequency also increases gradually.
3. Phase III (burst phase) lasts for 10 to 20 minutes. It includesintense and regular contractions for short period. It is due to this wave that all the undigested material is swept out of the stomach down to the small intestine. It is also known as the housekeeper wave.
4. Phase IV lasts for 0 to 5 minutes and occurs between phases III and I of 2 consecutive cycles.

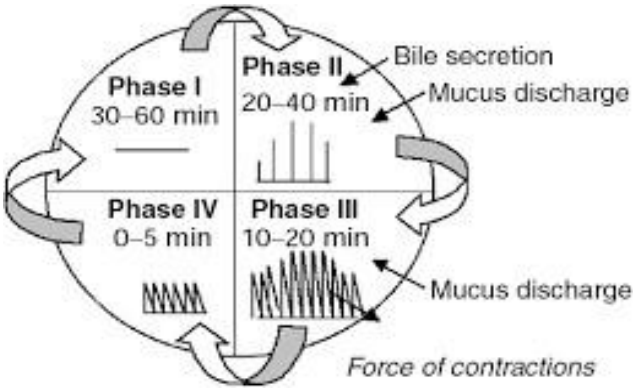


Fig 1.2: Motility pattern in GITGastroretentive Drug Delivery Systems.

Gastroretentive systems can remain in the gastric region for several hours and hence significantlyprolong the gastric residence time of drugs. Prolonged gastric retention improves bioavailability, reduces drug waste, and improves solubility for drugs that are less soluble in a high pH environment. It has applications also for local drug delivery to the stomach and proximal small intestines. Gastro retention helps to provide better availability of new products with new therapeutic possibilities and substantial benefits for patients.[11]

Need For Gastroretentive Drug Delivery System

Various drugs have their greatest therapeutic effect when released in the stomach, particularly when the release is prolonged in a continuous, controlled manner. Drugs delivered in this manner have a lower level of side effects and provide their therapeutic effects without the need for repeated dosages or with a low dosage frequency. Sustained release in the stomach is also useful for therapeutic agents that the stomach does not readily absorb, since sustained

release prolongs the contact time of the agent in the stomach or in the upper part of the small intestine, which is where absorption occurs and contact time is limited. Under normal or average conditions, for example, material passes through the small intestine in as little as 1-3 hours. Gastroretentive systems useful for drugs acting locally in the stomach (Antacids and drugs for H. Pylori viz., Misoprostol), Drugs that are primarily absorbed in the stomach (Amoxicillin), Drugs that is poorly soluble at alkaline pH (Furosemide, Diazepam, Verapamil), Drugs having narrow absorption window (Cyclosporine, Methotrexate, Levodopa), Drugs which are absorbed rapidly from the GI tract (Metonidazole, tetracycline), Drugs that degrade in the colon (Ranitidine, Metformin HCl), Drugs that disturb normal colonic microbes (antibiotics against Helicobacter pylori).[12.13]

Factors Controlling Gastroretention of Dosage Forms

The stomach anatomy and physiology contain parameters to be considered in the development of gastroretentive dosage forms. To pass through the pyloric valve in to the small intestine, the particle size should be in the range of 1 to 2 mm.[14] The most important parameters controlling thegastric retention time (GRT) of oral dosage forms include: density, size and shape of the dosage form, food intake and its nature, caloric content and frequency of intake, posture, gender, age, sex, sleep, body mass index, physical activity and diseased states of the individual (e.g. chronic disease, diabetes etc.) and administration of drugs with impact on gastrointestinal transit time for example drugs acting as anticholinergic agents (e.g. atropine, propantheline), Opiates (e.g. codeine) and prokinetic agents (e.g. metclopramide, cisapride). The molecular weight and lipophilicity of the drug depending on its ionization state are also important parameters.[15]

Types of gastroretentive system

a. High Density System: Sedimentation has been employed as a retention mechanism for pellets that are small enough to be retained in the folds of the stomach body near the pyloric region, which is the part of the organ with the lowest position in an upright posture.[16]

b. Modified Shape Systems/ Unfolding Systems: These are the dosage forms, which after swallowing, swell to an extent that prevent their exit from the pylorus. As a result, the dosage form is retained for a longer period of time.[17]

c. Mucoadhesive Systems: Bioadhesive drug delivery systems are used as a delivery device within the human to enhance drug absorption in a site-specific manner. In this approach, bio adhesive polymers are used and they can adhere to the epithelial surface in the stomach.

Thus, they improve the prolongation of gastricretention.[18] Materials commonly used for bioadhesion are poly acrylic acid, chitosan, cholestyramine, sodium alginate, hydroxypropyl methylcellulose (HPMC), sucralfate, tragacanth, dextrin, polyethylene glycol (PEG) and polylactic acids etc. Even though some of these polymers are effective at producing bioadhesive, it is very difficult to maintain it effectively because of the rapid turnover of mucus in the gastrointestinal tract (GIT).

d. Floating 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 gastric emptying rate for a prolonged period of time.

Floating drug delivery systems (FDDS) are aimed to retain the drug in thestomach and are useful for drugs that are poorly soluble or unstable in intestinal fluids. The underlying principle is very simple i.e., to make the dosage form less dense than the gastric fluids so that it can float on them. The density of the system can be reduced by incorporating a number of low density fillers in to the systems such as hydroxyl cellulose lactates or microcrystalline cellulose. However, this system is not ideal because its performance is highly dependent on the presence offood and fluid in the stomach. The basic idea behind the development of such a system was to maintain a constant level of drug in the blood plasma inspire of the fact that the drug dose not undergoes disintegration. The drug usually keeps floating in th gastric fluid and slowly dissolves at a predetermined rate to release the drug from the dosage form and maintain constant drug levels in the blood.[20] The concept of floating tablets is mainly based on the matrix type drug delivery system such that the drug remains embedded in the matrix which after coming incontact with the gastric fluid swells up and the slow erosion of the drug without disintegration of the tablet takes place. Sometimes for generating a floating system we even need to add some effervescent or gas generating agent which will also ultimately reduce the density of the system and serve the goalof achieving a floating system. These systems have a particular advantage that they 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 GIT. These systems continuously release the drug before it reaches the absorption window, thus ensuring optimalbioavailability. Different approaches are currently used to prolong the gastric retention time, like hydro dynamically balanced systems, swelling and expanding systems, polymeric bio-adhesive systems, modified shape systems, high density systems and other delayed gastric emptying devices. The principle of buoyant preparation offers a simple and practical approach to achieve increased gastric

residence time for the dosage form and sustained drug release.[21]

Based on the mechanism of buoyancy two distinctly different technologies

1. Non-effervescent system
2. Effervescent system

Non-effervescent system

In this system commonly used excipients are gel-forming or highly swellable cellulose type hydrocolloids, polysaccharides and matrix forming polymers such as polycarbonate, polyacrylate, polymethacrylate and polystyrene. One of the approaches to the formulation of such floating dosage forms involves intimate mixing of drug with a gel forming hydrocolloid which swells in contact with gastric fluid after oral administration and maintains a relative integrity of shape and a bulk density of less than unity within the outer gelatinous barrier. The air entrapped by the swollen polymer confers buoyancy to these dosage forms. The gel structure actsas a reservoir for sustained drug release since the drug is slowly released for sustained drug release since the drug is slowly released by a controlled diffusion through the gelatinous barrier.[22]

Effervescent system

These floating systems are prepared with swellable polymers such as methocel or polysaccharides like chitiosan and effervescent component containin sodium bicarbonate, citric and/or tartaric acid or matrices containing chambers of liquid that gasify at body temperature. The matrices are fabricated so that upon contact with gastric fluid, carbon dioxide is liberated by the acidity of gastric contents and is entrapped in the gelyfied hydrocolloid. This produces an upward motion of the dosage form and maintains its buoyancy. The carbon dioxide generating components may be intimately mixed within the tablet matrix to produce a single-layered tablet or a bi-layered tablet may be compressed which contains the gas generating mechanism in one hydrocolloid containing layer and the drug in the other layer formulated for the prolonged releaseeffect.[23]

Mechanism of floating systems: Various attempts have been made to retain the dosage form in the stomach as a way of increasing the retention time. FDDS have a bulk density less than gastricfluids 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.[24]

However, besides a minimal gastric content needed to allow the proper achievement of the buoyancy retention principle, a minimal level of floating force (F) is also required to keep the dosage form reliably buoyant on the surface of the meal. To measure the floating force kinetics, a novel apparatus for determination of resultant weight has been reported in the literature6. The apparatus operates by measuring continuously the force equivalent to F (as a function of time) that is required to maintain the submerged object. The object floats better if F is on the higher positive side.[25]

F = F buoyancy - F gravity = (Df - Ds) gvWhere,

F= total vertical force;

Df = fluid density;

Ds = object density;

v = volume and g = acceleration due to gravity

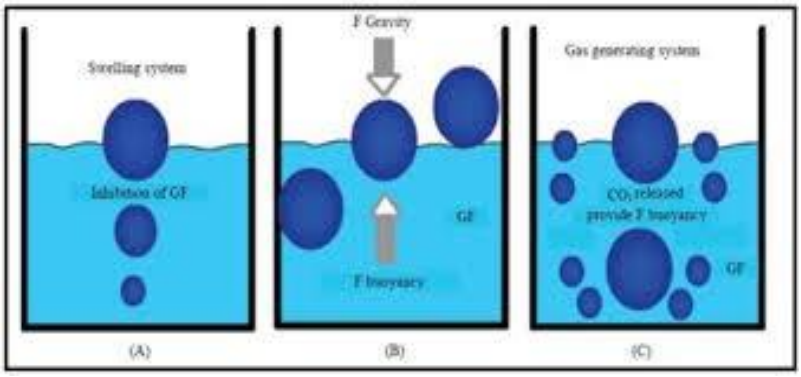


FIG 1.3: Mechanism of floating systems.

This apparatus helps in optimizing FDDS with respect to stability and durability of floating forces produced in order to prevent the drawbacks of unforeseeable intra-gastric buoyancycapability variations.

Advantages of FDDS

FDDS is highly advantageous in the treatment of the disorders related to the stomach. As the prime objective of such systems is to produce a gastro retentive product or a product which hasan enhanced retention time in the stomach.[26]

- Drugs with considerably short half life can be administered in this manner to get an appreciable therapeutic activity.

- Enhancement of the bioavailability for drugs which can metabolized in the upper GIT.
- They also have an advantage over the conventional system as it can be used to overcome the adversities of gastric retention time as well as the gastric emptying time.
- The duration of treatment through a single dose, which releases the anactive ingredient over an extended period of time
- The active entity is delivered specifically to the site of action, thus minimizing or eliminating the side effects.

Disadvantages of FDDS

- The major disadvantage of floating system is requirement of a sufficient high level of fluids in the stomach for the drug delivery to float. However this limitation can be overcome by coating the dosage form with the help of bioadhesive polymers that easily adhere to the mucosal lining of the stomach.[27]
- Gastric retention is influenced by many factors such as gastric motility, pH and presence of food. These factors are never constant and hence the buoyancy cannot be predicted.
- Drugs that cause irritation and lesion to gastric mucosa are not suitable to be formulated as floating drug delivery systems.
- High variability in gastric emptying time due to its all (or) non-emptying process.
- Patients should not be dosed with floating forms just before going to bed.
- Floating system is not feasible for those drugs that have solubility (or) stability problem in gastric fluids.
- The dosage form should be administered with a minimum of glass full of water (200-250 ml).
- The drugs, which are absorbed throughout GIT, which under go first-pass metabolism (Nifedipine, Propranolol etc.), are not desirable candidate.

Suitable drug candidates for FDDS

Various drugs have their greatest therapeutic effect when released in the stomach, particularly when the release is prolonged in a continuous, controlled manner. In general, appropriate candidates for FDDS are molecules that have poor colonic absorption but are characterized by better absorption properties at the upper parts of the GIT.[28]

- Drugs with narrow absorption window in GIT, e.g., Riboflavin and Levodopa
- Drugs that primarily absorbed from stomach and upper part of GIT, e.g., Calcium supplements, chlordiazepoxide and cinnarazine.

- Drugs that act locally in the stomach, e.g., Antacids and Misoprostol.
- Drugs that degrade in the colon, e.g., Ranitidine HCl and Metronidazole.
- Drugs that disturb normal colonic bacteria, e.g., Amoxicillin Trihydrate

Limitations of FDDS

1) Gastric retention is influenced by many factors such as gastric motility, pH and presence of food. These factors are never constant and hence the buoyancy cannot be predicted.

2) Drugs that cause irritation and lesion to gastric mucosa are not suitable to be formulated asfloating drug delivery systems.

3) High variability in gastric emptying time due to its all or non-emptying process.

4) Gastric emptying of floating forms in supine subjects may occur at random and becomes highly dependent on the diameter and size. Therefore patients should not be dosed with floating forms just before going to bed.[29]

Factors affecting floating drug delivery system

Various attempts have been made to retain the dosage form in the stomach as a way of increasing the retention time. These attempts include use of floating dosage forms (gasgenerating systems and swelling or expanding systems), mucoadhesive systems, highdensity systems, modified shape systems, gastric-emptying delaying devices and coadministrationof gastric-emptying delaying drugs. Most of these approaches are influenced by a number of factors that affect their bioavailability and efficacy of the gastro retentive system.

Density

gastric retention time (GRT) is a function of dosage form buoyancy that is dependent on thedensity.

Size

dosage form units with a diameter of more than 7.5 mm are reported to have an increased GRTcompared with those with a diameter of 9.9 mm.

Shape of dosage form

tetrahedron and ring shaped devices with a flexural modulus of 48 and 22.5 kilo pounds per square inch (KSI) are reported to have better GRT 90% to 100% retention at 24 hours

compared with other shapes.

Single or multiple unit formulation

Multiple unit formulations show a more predictable release profile and insignificant impairing of performance due to failure of units, allow co-administration of units with different releaseprofiles or containing incompatible substances and permit a larger margin of safety against dosage form failure compared with single unit dosage forms.

Fed or unfed state

Under fasting conditions, the GI motility is characterized by periods of strong motoractivity orthe migrating myoelectric complex (MMC) that occurs every 1.5 to 2 hours. The MMC sweeps undigested material from the stomach and, if the timing of administration of the formulation coincides with that of the MMC, the GRT of the unit can be expected to be very short. However, in the fed state, MMC is delayed and GRT is considerably longer.

Nature of meal

feeding of indigestible polymers or fatty acid salts can change the motility pattern of the stomachto a fed state, thus decreasing the gastric emptying rate and prolonging drug release.

Caloric content

GRT can be increased by four to 10 hours with a meal that is high in proteins and fats.

Frequency of feed

The GRT can increase by over 400 minutes when successive meals are given compared with asingle meal due to the low frequency of MMC.

Gender

mean ambulatory GRT in males (3.4±0.6 hours) is less compared with their age and race matched female counterparts (4.6±1.2 hours), regardless of the weight, height andbody surface).

Age

elderly people, especially those over 70, have a significantly longer GRT.

Posture

GRT can vary between supine and upright ambulatory states of the patients.

Concomitant drug administration

anticholinergics like atropine and propantheline, opiates like codeine and prokinetic agents likemetoclopramide and cisapride; can affect floating time.

Biological factors

Diabetes and Crohn's disease, etc.[30]

Polymers used in floating drug delivery[31,32]

Sustained Release Polymers are HPMC K100M, HPMC K15M, HPMC ELV, Polycarbonate,Polyethylene glycol, Sodium alginate, Carbopol, Eudragit.

Effervescent Generating System: Citric and Tartaric Acid, Sodium Bicarbonate, Citroglycine. Polymers which increase buoyancy: Ethyl cellulose Polymers which decrease release: Talc, Magnesium Stearate, Dicalcium Phosphate. Polymers which increase release: Mannitol, Lactose.

Inert Polymers: Long Chain Fatty Alcohol, Fatty Acid, Beeswax.Polymers with low density: Foam powder of polypropylene

Applications of floating drug delivery system[33]

Floating drug delivery offers several applications for drugs having poor bioavailability because of the narrow absorption window in the upper part of the gastrointestinal tract. It retains the dosage form at the site of absorption and thus enhances the bioavailability. These are summarized as follows.

Sustained Drug Delivery

HBS systems can remain in the stomach for long periods and hence can release the drug over a prolonged period of time. The problem of short gastric residence time encountered with an oral controlled release formulation hence can be overcome with these systems. These systems have a bulk density of <1 as a result of which they can float on the gastric contents. These systems are relatively large in size and passing from the pyloric opening is prohibited. Eg. Sustained release floating capsules of nicardipine hydrochloride were developed and were evaluated in vivo. The formulation compared with commercially available MICARD capsules using rabbits. Plasma concentration time curves showed a longer duration for administration (16 hrs) in the sustained release floating capsules as compared with conventional MICARD capsules (8 hrs).

Site-specific drug delivery

These systems are particularly advantageous for drugs that are specifically absorbed from stomach or the proximal part of the small intestine. E.g. Riboflavin and Furosemide. Furosemide is primarily absorbed from the stomach followed by the duodenum. It has been reported that a monolithic floating dosage form with prolonged gastric residence time was developed and the bioavailability was increased. AUC obtained with the floating tablets was approximately 1.8 times those of conventional Furosemide tablets.

Absorption Enhancement

Drugs that have poor bioavailability because of sites specific absorption from the upper part of the gastrointestinal tract are potential candidates to be formulated as floating drug delivery systems, thereby maximizing their absorption. Eg. A significantly increase in the bioavailability of floating dosage forms(42.9%) could be achieved as compared with commercially available LASIX tablets (33.4%) and enteric coated LASIX-long product (29.5%). The swelling behavior of a dosage form was measured by studying its weight gain or water uptake. The dimensional changes could be measured in terms of the increase in tablet diameter and/or thickness over time. Water uptake was measured in terms of percent weight gain, as given by the equation.

$WU = (W1 – W0)/ W0 \times 100$

Where, Wt = Weight of dosage form at time t.W0 = Initial weight of dosage form.

2. LITERATURE REVIEW

Aiswarya Patnaik et al., (2019) Formulation and Evaluation of Floating Tablet of Pantoprazole Sodium. The Present research work focuses on the formulation and evaluation of Floating tablet of Pantoprazole sodium. Floating tablets were prepared by direct compression method. 40mg of Pantoprazole was taken in a single tablet of 250mg. Floating tablet of pantoprazole sodium increase the gastric residence time as well as bioavailability and thereby showed increased therapeutic efficacy. The addition of gel forming polymer (HPMC) and gas generating agent sodium bicarbonate and citric acid was essential to achieve In vitro buoyancy. Preformulation studies were conducted to select suitable excipient, Combination of different excipient was used to formulate pantoprazole floating tablets. The evaluation parameter such as Weight variation, Thickness, Hardness, Friability, disintegration time, In-vitro drug release studies was conducted. The results were within the limit and were compared with marketed formulation.[34]

V. Sarovar Reddy et al., (2018) Formulation and Evaluation of Floating Tablets of Ciprofloxacin Hydrochloride. Formulation and evaluation of floating tablets of ciprofloxacin hydrochloride. Materials and Methods: In the present study the formulations were prepared by wet granulation technique using different proportions of hydroxypropyl methylcellulose (HPMC) K100M, HPMC K15M and Carbopol 934 as Swellable polymers. Citric acid has stabilizing effect and sodium bicarbonate is used as buoyancy-imparting agent. Results and Discussion: The prepared formulations were evaluated for different parameters during its pre-compression and Post-compression stages. The release characteristics of the formulations were studied in in-vitro conditions. The in-vitro dissolution study of formulation F4 was 99.12% within 12 h for good release and was fitted to kinetics of drug release for R2 value of korsmeyer-peppas model is 0.9854. The drug release was diffusion mediated and from the peppa's plot, it is confirmed that itis of non-fickian type. Conclusion: As an extension of this work for formulation F4, bioavailability, pharmacokinetic, and in vivo studies can be done in future to develop as suitable candidate for a novel drug delivery system.[35]

Nansri Saha et al.,(2018) Formulation And Evaluation Of Gastro Retentive Floating Tablets Of Nimodipine. Nimodipine is a dihydropyridine calcium channel blocker developed for the treatment of high blood pressure. Nimodipine has a half-life of 1.7-9 h, the bioavailability of 13% and it has narrow absorption window in upper part of the gastrointestinal tract (GIT), hence floating drug delivery system (FDDS) is preferred. Thus it is decided to prolong the gastric residence time in terms of making floating gastro retentive drug delivery system to increase drug absorption and hence bioavailability. In this study Nimodipine floating tablets were prepared by using two different techniques like Effervescent floating tablets and Non Effervescent floating tablets using Na-Carboxy methyl cellulose, Karaya gum and HPMC E5 as polymers and gas generating agents like sodium bicarbonate and citric acid and polypropylene foam powder as a selling agent in non-effervescent floating tablets. The tablets prepared by direct compression technique were evaluated in terms of their pre-compression parameters and post compression characteristics such as physical characteristics, total buoyancy, buoyancy lag time, swelling index and in vitro release. The best formulation showed no significant change in physical appearance, drug content, total buoyancy time, buoyancy lag time or in vitro release after storage at 40˚C /75% RH for three months. The in vitro release studies confirmed that the formulation (F6) containing 90 mg of karaya gum showed sustained drug release (99.01 ±0.28%) for 12 h and remained buoyant for more than 12 h.[36]

Ayesha Salma Habeeb et al.,(2018) Formulation and in vitro evaluation of captopril floating tablets by using natural polymers. Formulation and in vitro evaluation of captopril floating tablets by using natural polymers. The objective of this research is to formulate and develop gastroretentive floating matrix tablets of Captopril using natural polymers by effervescent system which will retain the drug upto 12 hours, to prepare and evaluate floating tablets of Captopril using natural polymers karaya gum, badam gum alone and in combination. Sodium bicarbonate is used as effervescent component, tablets were compressed using direct compression and wet granulation methods. The prepared tablets showed acceptable physicochemical characteristics, floating characteristics (floating lag time, floating time), swelling index, drug content and evaluated for in vitro release characteristics for 12hours in 0.1N HCl. Drug compatibility with excipients was checked by FTIR studies. Formulations with low concentration of polymers were unable to produce the desired action. The formulations prepared with combination of polymers (Karya gum+ Badam Gum) was retarding the drug release up to 12 hours (F11=96.68). From the release kinetics data it was evident that the formulation followed Higuchi release mechanism.[37]

Anas T et al.,(2018) Formulation And In Vitro Evaluation Of Amlodipine Gastroretentive Floating Tablets Using A Combination Of Hydrophilic And Hydrophobic Polymers.s.

Objective: The aim of this study was to formulate a developed floating tablet of amlodipineusing different concentrations and types of hydrophilic and hydrophobic polymers to be conserved in the stomach for modulating solubility and bioavailability, diminishes drug waste and decline side effects. Through this study, eleven innovative formulations of amlodipine floating tablets were prepared [mixture of amlodipine, sodium bicarbonate (NaHCO3), hydroxypropyl methylcellulose (HPMC) E50, HPMC K100M, ethylcellulose (EC) 5 mp. a. s.] by direct compression method. The pre-compressed mixtures were then evaluated for numerous parameters such as angle of repose, bulk density, tapped density, Carr's compressibility indexand Hausner's ratio. After compression, tablets were subjected to several tests like; floating behavior of tablets, tablet thickness, hardness test, friability test, weight variation, in vitrodissolution test. In addition, the optimum formulation was evaluated for Fourier transform- infrared (FT-IR) and differential scanning calorimetry (DSC) tests.From in vitro dissolution tests and kinetic assessments; F8 was selected as an optimum formula, depending on the R2 value of zero order kinetics (0.9915) and (n) value of Korsmeyer-Peppas (0.9635) which indicate purely relaxation zero order kinetic with good

delaying in drug release that was reached to 14 h.It can be concluded that the developed formulation of a certain combination of low viscosity grades of HPMC and EC was considered an efficient floating tablet.[38]

Bharat w. Tekade et al.,(2017) Formulation And In Vitro Evaluation Of Floating Tablets Of Cefpodoxime Proxetil. The objective of research work was to formulate and evaluate the floating drug delivery system containing Cefpodoxime Proxetil using polymer HPMC K4M, Guar Gum. Effervescent floating tablets containing Cefpodoxime proxetil were prepared by direct compression technique using varying concentrations of different grades of polymer Physical parameters like hardness, weight variation, thickness and friability were within pharmacopoeial limit. Percentage drug content in all floating tablet formulations was found to be 90% to 110%. The floating time was found to be more than 12 H. floating lag time was found to be 10±2.99 second. Formulation batch F8 was selected as an optimum formulation, as possessing less disintegration time, higher water absorption ratio and good content uniformity i.e. within acceptable limit.% drug release of formulation batch F8 was found to be 96.66% in 0.1 N HCL. The FT-IR studies of batch F8 was carried out which showed the peak values within the spectrum corresponding to the peak values of pure drug.[39]

Yerikala Ramesh et al.,(2017) Formulation And Evaluation Of Floating Drug Delivery Of Cefotaxime Using Raft Forming Approach. The cefotaxime is a broad spectrum cephalosporin antibiotic. It is mainly used in the treatment of bacterial infections. Cefotaxime is a suitable candidate for controlled release administration due to its short elimination time 1 hour. The main aim of the present investigation is to increase the gastric residence time by preparing floating drug delivery by using raft forming approach thereby improving bioavailability. The prepared Cefotaxime floating drug delivery by using raft forming approach were evaluated for hardness, weight variation, thickness, friability, drug content uniformity, total floating time, In-vitro dissolution studies and buoyancy lag time. Floating tablets were formulated using direct compression technique. Various polymers are used in the formulation they Micro crystalline cellulose used as binder, HPMC K15M, Guargum used as hydrophilic polymers, Chitosan,Sodium bicarbonate was incorporated as an effervescent substance, Sodium alginate used as viscous gel forming agent, Magnesiu streate used as lubrication, talc was used as diluent. The formulated Cefotaxime tablet to be evaluated the following parameters as follow Weight variation (mg), Hardness, Thickness, Friability, Drug content uniformity, Floating lag time, the in vitro cumulative amount of drug released was

shown the F7 is 99.28% within 45 minutes the comparative studies with marketed formulations F7 show the better results.[40]

Mourya Adarsh et al.,(2017) Design formulation and evaluation of gastroretentive floating tablets of stavudine. The purpose of the present research work was to design, formulate and evaluate the floating tablets of Stavudine, a gastro retentive drug delivery system. Direct compression was used to prepare the tablets using HPMC K4M, HPMC K15M and Carbopol 974(p) as polymers. Formulations were prepared by varying the amount of polymers. The compatibility of drug with the polymers is identified by using FTIR studies. Gastric floating of Stavudine tablets results from effervescence produced by the reaction between sodium bicarbonate and hydrochloric acid in stomach. Twelve formulations of floating tablets were prepared using direct compression technique with polymer such as carbopol974 (p), HPMC grades, Xanthium gum, Guar gum, chitosan in different ratios. The evaluation results revealed that all formulations comply with the specification of official pharmacopoeias and/or standard reference with respect to general appearance, content uniformity, hardness, friability and buoyancy. Out of all theformulation developed, formulation F8 containing of Carbopol showed invitro drug release of 97.8% up to desired time period of i.e., 24 hours. Thus it is summarized; carbopol grades can be used in formulation of gastro retentive floating drug delivery system. Thecompatibility of drug with polymers is identified by FT-IR studies. The resultsobtained showed that the drug is compatible with all the polymers used. The prepared tablets (F1-F12) were evaluated for both pre-compression and post-compression parameters. The results obtained showed that the drug is compatible with all the polymers used.[41]

Md. Haider Ali et al.,(2016) Formulation and In vitro Evaluation of Oral Floating Tablets of Salbutamol Sulphate: Comparison with Effervescent Tablets. The aim of this research was to develop and evaluate gastric floating tablets of salbutamol sulphate. The oral delivery of anti-asthmatic salbutamol sulphate tablets were facilitated by preparing floating dosage form which could increase its absorption in the stomach by increasing the gastric residence time of the drug. Floating tablets were formulated by using different polymers like carbopol, xanthan gum, HPMC-K4 MCR and HPMC- K100 MCR with different proportions. A comparative study of normal effervescent tablets of salbutamol sulphate had also been done. The prepared tablets wereevaluated for all their physicochemical properties and in vitro buoyancy study. In vitro dissolution studies of the formulations were done in pH 6.8 phosphate buffer using USP

apparatus 2 (paddle method) at 50 rpm. Percent drug release of the formulations (F-1 to F-11) was from 87.34%- 99.12% after 12 hours. From the results, F-11 was selected as an optimized formulation based on 12 h drug release which showed minimal floating lag time and maximum floating time. On the other hand, 100% drug was released within 2 hours from the F-12 of effervescent salbutamol sulphate tablets in which polymer was absent while gas generating sodium bicarbonate and citric acid were present. The results of the study were consistent andmay encourage formulating similar dosage form with other drugs.[42]

Ramu Bandameedi et al.,(2015) Formulation and Evaluation of Floating Osmotic Tablets of Nizatidine. This study was conducted to develop floating osmotic tablets of Nizatidine, a H2 receptor antagonist, to release the drug as two distinct pulses separated by a lag time that achieve plasma concentration profiles varying in a circadian rhythm fashion, for the chronotherapy of ulcer. Floating osmotic tablets were developed using effervescence method consisted of three different steps viz, preparation of floating sustained release drug containing tablets followed by time-lagged (4 hrs) coating with hydrophobic rupturable polymer, ethyl cellulose (EC), and finally compression coating with immediate release dose of nizatidine and supporting buoyant layer. Three ratios of Ethyl cellulose to HPMC E15 (32.5:67.5, 50:50, and 67.5:32.5) at three coating levels (5%, 10%, 15%) were used to optimize the lag time (4 hrs). Carbopol 934P, cross povidone and sodium bicarbonate were used in buoyant layer. The developed floating osmotic tablets by effervescence method were evaluated for preformulation parameters, weight variation, thickness, hardness, friability, drug content, content uniformity, In-vitro floating properties, and In-vitro drug release. The optimized formulation provided expected two-phase release pattern of Nizatidine with initial immediate dose release in 30 min and then lag time 4 hrs of no drug release followed by sustained release for 8hrs in stomach during floating.[43]

Shiva lakshmaiah et al.,(2014) Formulation and evaluation of hydrodynamically balanced floating tablets of antidiabetic agent. The objective of the present study was to develop a hydrodynamically balanced system of metformin as a single unit floating tablet. Various grades of low-density polymers such as HPMC K4M, HPMC K 15M and Polyethylene oxide were used in different concentrations along with gas generating agent sodium bicarbonate and tablets were prepared by using direct compression technique to study the effect these polymers on floating behaviors. The physicochemical properties of different formulations, their buoyancy lag time and total floatation time and swelling index were evaluated. It is

found that the high viscosity grade polymers given better controlled release drug profile. The in vitro release studies indicated that the floating dosage forms containing (P3) polyethylene oxide polymer showed good drug releaserate up to 12hrs in comparison to other batches. The results indicated that hydrodynamically balanced tablets of Metformin containing polyethylene oxide provides a better option for sustained release action.[44]

L. Kukati, K et al.,(2014) Formulation And Evaluation Of Floating Tablets Of Cefpodoxime Proxetil. In the present investigation, an attempt was made to develop gastro retentive tablets of cefpodoxime proxetil (CP) using locust bean gum as release retarded material. CP is an orally administered, extended spectrum, semi-synthetic antibiotic of cephalosporin class. CP has a short elimination half-life and also possesses high solubility, chemical, enzymatic stability and absorption profiles in acidic pH which makes CP suitable candidate for formulating it as gastro retentive dosage form for improved bioavailability. Sodium bicarbonate and citric acid were usedas effervescent agents to get desired floating properties. The tablets prepared were evaluated and found to have acceptable physicochemical properties. The in vitro release data of optimized formulation was treated with mathematical equations and was concluded that drug release followed zero order kinetics with anomalous transport mechanism. Based on the results it can be concluded that floating tablets of cefpodoxime proxetil containing locust bean gum provides a better option for controlled release action and improved bioavailability.[45]

3. AIM AND OBJECTIVESAIM

The aim of the present work is to Formulation and *in vitro* Evaluation of Floating Tablets of Lansoprazole for the Treatment of Anti-ulcer agents.

OBJECTIVES

The gastro retentive drug delivery systems can be retained in the stomach and assist in improvingthe oral sustained delivery of drugs that have an absorption window in a particular region of gastrointestinal tract. These systems help in continuously releasing the drug before it reaches the absorption window, thus ensuring optimal bioavailability. And also cost effective process.

As a PPI, Lansoprazole is a prodrug and requires protonation via an acidic environmentto become activated. Once protonated, lansoprazole is able to react with cysteine residues, specifically Cys813 and Cys321, on parietal H+,K+-ATPase resulting in stable

disulfides. PPI's in general are able to provide prolonged inhibition of acid secretion due to their ability to bind covalently to their targets.

In the present investigation floating tablets of Lansoprazole were prepared by direct compression.

4. PLAN OF WORK

1. Literature Survey
2. Selection and Procurement of suitable Drug candidate and Excipients
3. Preparation of standard graph of Lansoprazole in 0.1 N HCL
4. Drug and Excipient compatibility studies using FTIR
5. Formulation of floating tablets of Lansoprazole

A. Formulation development of Lansoprazole floating tablets using Naturalpolymers

6. Precompression studies of Formulation blend of F1 – F9

A. Angle of repose
B. Bulk density
C. Tapped density
D. Carr's index
E. Hausner's ratio

7. Preparation of the Floating tablets of Lansoprazole
8. Post Compression Evaluation of prepared floating tablets of Lansoprazole

A. Weight variation
B. Tablet Thickness
C. Tablet Hardness
D. Friability
E. Assay
F. *In-vitro* buoyancy studies

i. Floating lag time
ii. Total Floating time

G. *In vitro* release studies

9. Selection of optimised formulation
10. Kinetic analysis of Optimised dissolution data

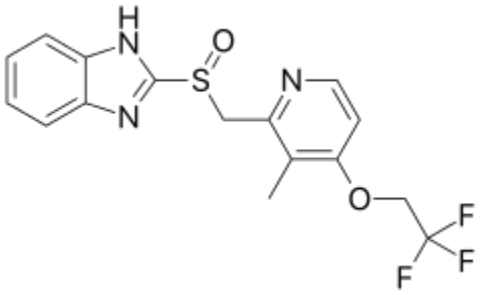
5. DRUG PROFILE

Drug: Lansoprazole

Synonym: Lansoprazol

Drug category: Anti-Ulcer Agents

Structure



Chemical name/ Nomenclature / IUPAC Name: (RS)-2-([3-methyl-4-(2,2,2-trifluoroethoxy)pyridin-2-yl]methylsulfinyl)-1H-benzo[d]imidazole.

Molecular Formula: C16H14F3N3O2S

Molecular Weight: 369.363 gm/mole.

Official Pharmacopoeia: USP

PHYSICOCHEMICAL PROPERTIES:

Description(Physical State): Solid

Solubility: water solubility 0.97 mg/L

Dosage: Capsule

Melting point: 178-182 °C

Log P: 1.9

PHARMACOKINETIC PROPERTIES:

Bioavailability: 80% or more

Half-life: 1.5 (± 1.0) hours

Absorption: The absorption of lansoprazole is rapid, with mean Cmax occurring approximately 1.7 hours after oral dosing, and relatively complete with absolute bioavailability over 80%.

Protein binding: 97%

Metabolism: Hepatic. Two metabolites have been identified in measurable quantities in

plasma (the hydroxylated sulfinyl and sulfone derivatives of lansoprazole). These metabolites have very little or no antisecretory activity. Lansoprazole is thought to be transformed into two active species which inhibit acid secretion by (H+,K+)-ATPase within the parietal cell canaliculus, but are not present in the systemic circulation.

Excretion: Following single-dose oral administration of PREVACID, virtually no unchanged lansoprazole was excreted in the urine. In one study, after a single oral dose of 14C-lansoprazole, approximately one-third of the administered radiation was excreted in the urine and two-thirds was recovered in the feces. This implies a significant biliary excretion of the lansoprazole metabolites.

Adverse effects/Side effects: Dizziness, Fast or irregular heart rate, Watery or bloody diarrhea.

PHARMACODYNAMICS: Lansoprazole, an acid proton-pump inhibitor similar to omeprazole, is used as an untiulcer drug in the treatment and maintenance of healing of duodenal or gastric ulcers, erosive and reflux esophagitis, NSAID-induced ulcer, Zollinger-Ellison syndrome, and Barrett's esophagus. Lansoprozole is active against Helicobacter pylori. The plasma elimination half-life of lansoprazole does not reflect its duration of suppression of gastric acid secretion. Thus, the plasma elimination half-life is less than two hours, while the acid inhibitory effect lasts more than 24 hours.

Mechanism of action: Lansoprazole belongs to a class of antisecretory compounds, the substituted benzimidazoles, that do not exhibit anticholinergic or histamine H2-receptor antagonist properties, but rather suppress gastric acid secretion by specific inhibition of the (H+,K+)-ATPase enzyme system at the secretory surface of the gastric parietal cell. Because this enzyme system is regarded as the acid (proton) pump within the parietal cell, Lansoprazole has been characterized as a gastric acid-pump inhibitor, in that it blocks the final step of acid production. This effect is dose-related and leads to inhibition of both basal and stimulated gastricacid secretion irrespective of the stimulus.

Therapeutic efficacy/ Indications: For the treatment of acid-reflux disorders (GERD), peptic ulcer disease, H. pylori eradication, and prevention of gastroinetestinal bleeds with NSAID use.

Contraindications: Proton pump inhibitors (PPIs) hypersensitivity, Vitamin B12 deficiency,

Hepatic disease.

INTERACTIONS

Drug interactions

- ✓ 4-Methoxyamphetamine The metabolism of 4-Methoxyamphetamine can be decreased when combined with Lansoprazole.
- ✓ 5-androstenedione The metabolism of 5-androstenedione can be increased when combined with Lansoprazole.
- ✓ 6-Deoxyerythronolide B The metabolism of Lansoprazole can be decreased when combined with 6-Deoxyerythronolide B.
- ✓ 6-O-benzylguanine The metabolism of 6-O-benzylguanine can be increased when combined with Lansoprazole.

Food interactions

- ✓ Avoid alcohol.
- ✓ Food reduces bioavailabilty, but this has very little clinical impact.

DRUG FORMULATION

S.No	Drug name	Label Claim	Brand name	Company
1	Lansoprazole	15mg	Prevacid	Mylan

6. EXCIPIENTS PROFILEXANTHAN GUM

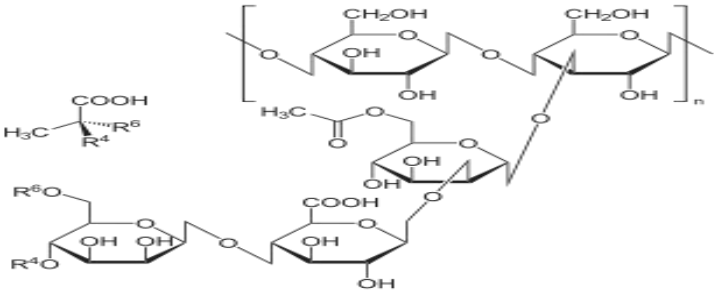
Nonproprietary Names

- ❖ BP and USP/NF: Xanthan gum
- ❖ PhEur: Xanthani gummi

Chemical Name: Xanthan gum

Synonyms: Corn sugar gum, E415, Keltrol, polysaccharide B-1459, Rhodigel, Vanzan, NF,Xantural.

Chemical structure



Molecular formula: $(C_{35}H_{49}O_{29})$ n

Molecular mass: 933(monomer)

Description

Odour: Odourless

Colour: White to cream coloured free flowing powder

Taste: Tasteless

Functional Category

- Stabilizing agent
- Suspending agent
- Viscosity-increasing agent.

Solubility: Practically insoluble in ethanol and ether, soluble in cold or warm water.

Melting point: Chars at 270^0C.

Viscosity (dynamic): 1200–1600mPa s (1200–1600cP) for a 1%w/v aqueous solution at 25^0C.

Stability and Storage Conditions

Xanthan gum is a stable material. Aqueous solutions are stable over a wide pH range (pH3–12), although they demonstrate maximum stability at pH 4–10 and temperatures of 10–60^0C. Xanthan gum solutions of less than 1%w/v concentration may be adversely affected by higher than ambient temperatures, for example viscosity is reduced. Solutions are also stable in the presence of enzymes, salts, acids and bases.

The bulk material should be stored in a well-closed container in a cool, dry place.

Applications

- ✓ Xanthan gum is widely used in oral and topical pharmaceutical formulations, cosmetics and foods as a suspending and stabilizing agent.
- ✓ It is also used as a thickening and emulsifying agent.
- ✓ Xanthan gum has also been used to prepare sustained-release matrix tablets.
- ✓ Controlled-release tablets of diltiazem hydrochloride prepared using xanthan gum have been reported to sustain the drug release in a predictable manner.
- ✓ Xanthan gum has been incorporated in an ophthalmic liquid dosage form.
- ✓ Xanthan gum can be used to increase the bio adhesive strength in vaginal formulations and as a binder in colon specific drug delivery systems.
- ✓ Xanthan gum is also used as a hydrocolloid in the food industry and in cosmetics it has been used as a thickening agent in shampoo.

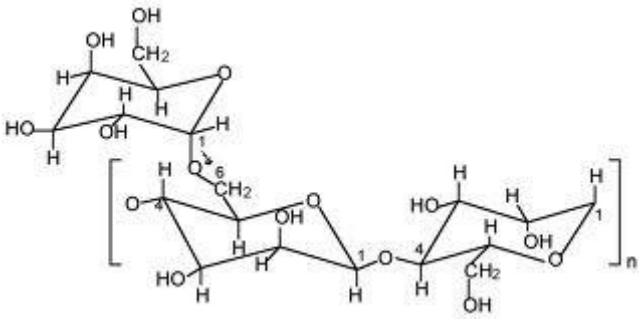
GUAR GUM

General Descriptions

Guar gum is a galactomannan, obtained from plant Cyamopsis tetragonolobus.

Description: Powder is whitish and yellowish consisting of slight odor. Guar gum is mainly consisting of the high molecular weight polysaccharides composed of galactomannans which are consisting of a linear chain of (1→4)-linked β-D-mannopyranosyl units with (1→6)-linked α-D- galactopyranosyl residues as side chains. The mannose: galactose ratio is approximately 2:1. Themolecular weight range is 50,000-8,000,000.

Structural Formula



Structure of Guar Gum

Functional categories: It has wide applications in Pharmaceutical formulations, Cosmetic,

Food, Textile, Paper, Explosive, Toiletries industries etc. In Pharmaceuticals, it is used as tablet binder and disintegrant, suspending, thickening and stabilising agent, as a controlled release carrier.

Solubility: Guar gum is more soluble than locust bean gum and is a better stabilizer, as it has more galactose branch points. Unlike locust bean gum, it is not self-gelling. However, eitherborax or calcium can cross-link guar gum, causing it to gel. In water, it is nonionic and hydrocolloidal. It is not affected by ionic strength or pH, but will degrade at pH extremes at temperature (e.g. pH 3 at 50 °C).It remains stable in solution over pH range 5-7. Strong acids cause hydrolysis and loss of viscosity, and alkalies in strong concentration also tend to reduce viscosity. It is insoluble in most hydrocarbon solvents.

Viscosity (dynamic): Guar gum shows high low-shear viscosity but is strongly shear-thinning. It is very thixotropic above 1% concentration, but below 0.3%, the thixotropy is slight. It has much greater low-shear viscosity than that of locust bean gum, and also generally greater than that of other hydrocolloids. Guar gum shows viscosity synergy with xanthan gum. Guar gum andmicellar casein mixtures can be slightly thixotropic if a biphase system forms.

Stability and Storage Condition

Aqueous guar gum dispersions have a buffering action and are stable at pH 4-10.5. The bacteriological stability of guar gum dispersion may be improved by addition of mixture of 0.15% methyl paraben and 0.02% propyl paraben as preservatives. It should be stored in well closed container in cool and dry place.

SODIUM ALGINATE

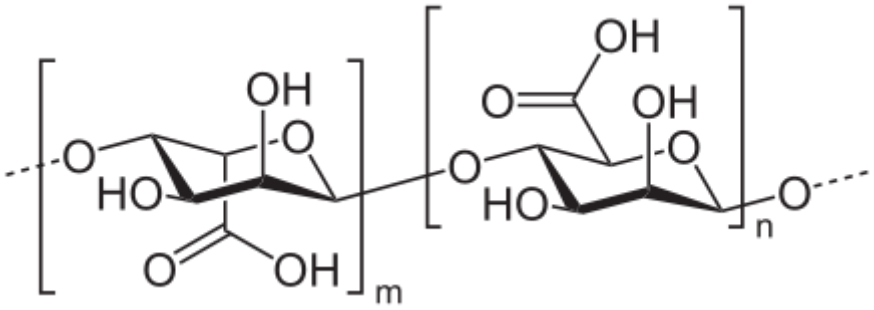
General Descriptions

Nonproprietry Names: BP: Sodium Alginate PhEur: Sodium Alginate USP-NF: Sodium Alginat.

Synonyms:. Alginato sodico; algin; alginic acid, sodium salt; E401; Kelcosol; Keltone; natriialginas; Protanal; sodium polymannuronate.

Description: It Sodium alginate occurs as an odorless and tasteless, white to pale yellowish-brown colored powder.

Structural Formula



Functional categories: Stabilizing agent; suspending agent; tablet and capsule disintegrant; tablet binder; viscosity increasing agent.

Viscosity (dynamic):sodium alginate show A wide range of viscosity types are commercially available. Aqueous solutions are most commonly prepared, although sodium alginate may also be dissolved in aqueous alcohols such as ethanol and propan-2-ol provided the alcohol content is less than 50% w/w.

pH: 5.5 – 8.0 for a 1 % w/w aqueous solution.

Melting point: Brown at 190- 200^{0}C; chars at 225-230^{0}C.

Specific gravity: 1.26

Loss on drying: < 5.0 %

Density (bulk): 0.341 gm / cm^3

Density (tapped): 0.557 gm / cm^3

Stability and storage Conditions Sodium alginate is a hygroscopic material, although it is stable if stored at low relative humidities and a cool temperature. Aqueous solutions of sodium alginate are most stable at pH 4–10. Below pH 3, alginic acid is precipitated. A 1% w/v aqueous solution of sodium alginate exposed to differing temperatures had a viscosity 60–80% of its original value after storage for 2 years.(39) Solutions should not be stored in metal containers.

Incompatibilities: Sodium alginate is incompatible with acridine derivatives, crystal violet, phenylmercuric acetate and nitrate, calcium salts, heavy metals, and ethanol in concentrations greater than 5%. Low concentrations of electrolytes cause an increase in viscosity but high electrolyte concentrations cause salting-out of sodium alginate; salting-out occurs if more than 4% of sodium chloride is present.

SODIUM BICARBONATE

Non-proprietary names: BP/EP: sodium bicarbonate

Synonym: Baking soda, e-500, and monosodium carbonate.

Chemical name: carbonic acid, monosodium salt, monosodium carbonate.

Empirical formula: NaHCO3

Molecular weight: 84.01

Category: alkalizing agent, therapeutic agent.

Description: it is an odorless, white crystalline powder with slight alkaline taste.

Acidity/ alkalinity: pH 8.3 for freshly prepared 0.1m aqueous solution at 250c.

Density: 2.159 g/cm3

Solubility: Soluble in water, practically insoluble in ethanol.

Stability and storage: Sodium bicarbonate is stable in dry air but slowly decomposes in Moist air and should therefore be stored in well-closed container in a cool dry place.

Safety: Orally ingested sodium bicarbonate neutralizes gastric acid with the evolution of carbon dioxide and may cause stomach cramps and flatulence.

Applications

Employed as a source of carbon dioxide in effervescent tablets and granules. Also used to buffer the drug molecules that are weak acids.

Used in solutions as buffering agent. Also used as freeze-drying stabilizer. As a gas forming agent.

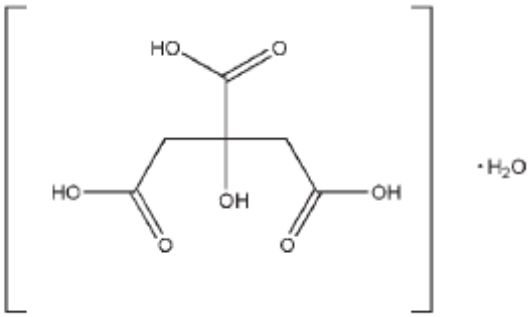
CITRIC ACID

BP: Citric Acid Monohydrate, JP: Citric Acid Hydrate, PhEur: Citric Acid Monohydrate, USP:Citric Acid Monohydrate.

Synonyms

Acidum citricum monohydricum; E330; 2-hydroxypropane-1,2,3- tricarboxylic acid monohydrate.

Empirical Formula: C6H8O7_H2O**Molecular Weight:** 210.14 **Structural Formula**



Functional Category

Acidifying agent; antioxidant; buffering agent; chelating agent; flavor enhancer; preservative.

Applications in Pharmaceutical Formulation or Technology

Citric acid (as either the monohydrate or anhydrous material) is widely used in pharmaceutical formulations and food products, primarily to adjust the pH of solutions. It has also been used experimentally to adjust the pH of tablet matrices in enteric-coated formulations for colon- specific drug delivery. Citric acid monohydrate is used in the preparation of effervescent granules, while anhydrous citric acid is widely used in the preparation of effervescent tablets.(2–4) Citric acid has also been shown to improve the stability of spray-dried insulin powder in inhalation formulations.

Description

Citric acid monohydrate occurs as colorless or translucent crystals, or as a white crystalline, efflorescent powder. It is odorless and has a strong acidic taste. The crystal structure is orthorhombic.

Incompatibilities

Citric acid is incompatible with potassium tartrate, alkali andalkaline earth carbonates and bicarbonates, acetates, and sulfides.Incompatibilities also include oxidizing agents, bases, reducingagents, and nitrates. It is potentially explosive in combination withmetal nitrates. On storage, sucrose may crystallize from syrups inthe presence of citric acid.

Stability and Storage Conditions

Citric acid monohydrate loses water of crystallization in dry air or when heated to about 408 C. Itis slightly deliquescent in moist air. Dilute aqueous solutions of citric acid may ferment on standing.

Safety

Citric acid is found naturally in the body, mainly in the bones, and is commonly consumed as part of a normal diet. Orally ingested citric acid is absorbed and is generally regarded as a nontoxic material when used as an excipient. However, excessive or frequent consumption of citric acid has been associated with erosion of the teeth.

AEROSIL

Synonyms: Colloidal silica, fumed silica, light anhydrous silicic acid, fumed, silicic anhydride, silicon dioxide.

Chemical name: Silica

Empirical formula: SiO2

Molecular weight: 60.08 daltons

Structural formula: SiO2

Functional category: Adsorbent, anticaking agent, emulsion stabilizer, glidant, suspending agent, tablet disintegrant, thermalstabilizer, viscosity-increasing agent.

Description: Colloidal silicon dioxide is submicroscopic fumed silica with a particle size of about 15 nm. It is a light, loose, bluish-white-colored, odorless, tasteless, non gritty amorphous powder.

Solubility: Practically insoluble in organic solvents, water, and acids, except hydrofluoric acid; soluble in hot solutionsof alkali hydroxide forms a colloidal dispersion with water.

Storage: Colloidal silicon dioxide powder should be stored in a wellclosed container.

Applications: Colloidal silicon dioxide is widely used in pharmaceuticals, cosmetics, and food products.

MAGNESIUM STEARATE

Synonyms: Magnesium octadecanoate; octadecanoic acid, magnesium salt; stearic acid, magnesium salt.

Molecular weight: 591.34.

Structural formula: $[CH_3(CH_2)_{16}COO]_2Mg$

Functional category: Tablet and capsule lubricant

Applications in pharmaceutical formulation technology: It is primarily used as a lubricant in capsule and tablet manufacture at concentrations between 0.25 % and 5.0 % w/w.

Description: Magnesium stearate is a fine, white, precipitated or milled, impalpable powder of low bulk density, having a faint odor of stearic acid and a characteristic taste. The powder is greasy to touch and readily adheres to the skin.

Crystalline forms: High purity magnesium stearate has been isolated as a trihydrate, dihydrate and an anhydrate.

Flowability: Poorly flowing, cohesive powder.

Melting range: 117-150^{o} C (commercial samples) 126-130^{o} C (high purity magnesium stearate).

Solubility: Practically insoluble in ethanol, ethanol (95 %), ether and water; slightly soluble in warm benzene and warm ethanol (95 %).

Specific surface area: 1.6-14.8 m^2 /g

Density (bulk): 0.159 g/cm^3

Density (tapped): 0.286 g/cm^3

Density (true): 1.092 g/cm^3

Stability and Storage Conditions: Magnesium stearate is stable and should be stored in a well-closed container in a cool, dry place.

Incompatibilities: Incompatible with strong acids, alkalis and iron salts strong oxidizing materials. Magnesium stearate cannot be used in products containing aspirin, some vitamins and most alkaloid salts.

Method of manufacture: Magnesium stearate is prepared either by the interaction of

aqueous solutions of magnesium Chloride with sodium stearate or by the interaction of magnesium oxide,hydroxide or carbonate with stearic acid at elevated temperatures.

Safety: Magnesium stearate is widely used as a pharmaceutical excipient and is generally regarded as being nontoxic following oral administration. However, oral consumption of large quantities mayresult in some laxative effect or mucosal irritation.

Microcrystalline cellulose

Synonyms: Avicel PH; Celex; cellulose gel; Celphere; Ceolus KG; crystalline cellulose; E460;Emcocel; Ethispheres.

Chemical Name: Cellulose.

Empirical Formula: $(C_6H_{10}O_5)n$ where $n \approx 220$.

Molecular Weight: ≈36 000

Functional Category: Adsorbent; suspending agent; tablet and capsule diluent; tablet disintegrant.

Applications: Microcrystalline cellulose is widely used in pharmaceuticals, primarily as a binder/diluent in oral tablet and capsule formulations where it is used in both wet-granulation and direct-compression processes. In addition to its use as a binder/diluent, microcrystalline cellulose also has some lubricant and disintegrant properties that make it useful in tableting. Microcrystalline cellulose is also used in cosmetics and food products.

Table 6.1: Uses Of Microcrystalline Cellulose.

Use	Concentration (%)
Adsorbent	20–90
Anti adherent	5–20
Capsule binder/diluents	20–90
Tablet disintegrant	5–15
Tablet binder/diluents	20–90

Description: cellulose is a partially cellulose that white, Microcrystalline purified, depolymerized occurs as a odorless, tasteless, crystalline powder composed of porous particles. It is commercially available indifferent particle sizes and moisture grades that have different properties and application.

Angle of repose (θ): 34.4°

Density (bulk): 0.337 g/cm^3 for Avicel P^H 200, 0.32 g/cm^3 for Avicel P^H 101

Density (tapped): 0.478 g/cm^3 for Avicel 200 0.45 g/cm^3 for Avicel P^H-101

Density (true): 1.512–1.668 g/cm^3

Flowability: 1.41 g/s

Melting point: 260–270°C.

Moisture content: Typically less than 5% w/w. microcrystalline cellulose is hygroscopic.

Particle size distribution: Typical mean particle size is 20–200 µm.

Solubility: Slightly soluble in 5% w/v sodium hydroxide solution; practically insoluble in water,dilute acids.

Specific surface area: 1.21–1.30 m^2/g for Avicel P^H-101 0.78–1.18 m^2/g for Avicel P^H-200.

Stability: Microcrystalline cellulose is a stable though hygroscopic material.

Storage Conditions: The bulk material should be stored in a well-closed container in a cool,dry place.

Safety: It is widely used in oral pharmaceutical formulations is generally regarded as a relatively nontoxic and nonirritant material. Deliberate abuse of formulations containing cellulose, either by inhalation or by injection, has resulted in the formation of cellulose granulomas.

7. METHODOLOGY

7.1.Analytical method development

a) Determination of absorption maxima

A solution containing the concentration 10µg/mL drug was prepared in 0.1N HCL UV spectrum was taken using Double beam UV/VIS spectrophotometer. The solution was scanned in the rangeof 200 – 400 nm.

b) Preparation calibration curve

10mg Lansoprazole pure drug was dissolved in 10ml of methanol (stock solution1) from stock solution 1ml of solution was taken and made up with10ml of 0.1N HCL (100µg/ml). From this 1ml was taken and made up with 10 ml of 0.1N HCL (10µg/+ml). The above solution was subsequently diluted with 0.1N HCL to obtain series of dilutions Containing 5, 10, 15, 20, 25 µg /ml of per ml of solution. The absorbance of the above dilutions was measured at 288nm 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.

7.2.Preformulation parameters

The quality of tablet, once formulated by rule, is generally dictated by the quality of physicochemical properties of blends. There are many formulations and process variables involved in mixing and all these can affect the characteristics of blends produced. The various characteristics of blends tested as per Pharmacopoeia.

Angle of repose

The frictional force in a loose powder can be measured by the angle of repose. It is definedas, the maximum angle possible between the surface of the pile of the powder and the horizontal plane. If more powder is added to the pile, it slides down the sides of the pile until the mutual friction of the particles producing a surface angle, is in equilibrium with the gravitational force. The fixed funnel method was employed to measure the angle of repose. A funnel was secured with its tip at a given height (h), above a graph paper that is placed on a flat horizontal surface.

The blend was carefully pored through the funnel until the apex of the conical pile just touches thetip of the funnel. The radius (r) of the base of the conical pile was measured. The angle of repose was calculated using the following formula.

$\tan \theta = h / r$ $\tan \theta$ = Angle of repose

h = Height of the cone, r = Radius of the cone base

Table 7.1: Angle of Repose values (as per USP).

Angle of Repose	Nature of Flow
<25	Excellent
25-30	Good
30-40	Passable
>40	Very poor

Bulk density

Density is defined as weight per unit volume. Bulk density, is defined as the mass of the powder divided by the bulk volume and is expressed as gm/cm^3. The bulk density of a powder primarily depends on particle size distribution, particle shape and the tendency of particles to adhere together. Bulk density is very important in the size of containers needed for handling, shipping, and storage of raw material and blend. It is also important in size blending equipment. 10 gm powder blend was sieved and introduced into a dry 20 ml cylinder, without compacting. The powder was carefully leveled without compacting and the unsettled apparent volume, Vo, was read.

The bulk density was calculated using the formula:Bulk Density = M / V_O

Where, M = weight of sample

V_O = apparent volume of powder

Tapped density

After carrying out the procedure as given in the measurement of bulk density the cylinder containing the sample was tapped using a suitable mechanical tapped density tester that provides 100 drops per minute and this was repeated until difference between succeeding measurement is less than 2 % and then tapped volume, V measured, to the nearest graduated unit.

The tapped density was calculated, in gm per L, using the formula.

Tap = M / V Where, Tap= Tapped Density

M = Weight of sample

V= Tapped volume of powder

Measures of powder compressibility

The Compressibility Index (Carr's Index) is a measure of the propensity of a powder to be compressed. It is determined from the bulk and tapped densities. In theory, the less

compressible a material the more flowable it is. As such, it is measures of the relative importance of interparticulate interactions. In a free- flowing powder, such interactions are generally lesssignificant, and the bulk and tapped densities will be closer in value.

For poorer flowing materials, there are frequently greater interparticle interactions, and a greater difference between the bulk and tapped densities will be observed. These differences are reflected in the Compressibility Index which is calculated using the following formulas:

Carr's Index = [(tap - b) / tap] × 100

Where, b = Bulk Density Tap = Tapped Density

Table 7.2: Carr's index value (as per USP).

Carr's index	Properties
5 – 15	Excellent
12 – 16	Good
18 – 21	Fair to Passable
2 – 35	Poor
33 – 38	Very Poor
>40	Very Very Poor

7.3.Formulation development of floating Tablets

For optimization of sodium bicarbonate concentration, granules were prepared by direct compression method.

Procedure for direct compression method

1) Drug and all other ingredients were individually passed through sieve no 60.
2) All the ingredients were mixed thoroughly by triturating up to 15 min.
3) The powder mixture was lubricated with talc.
4) The tablets were prepared by using direct compression method by using 6 mm punch.

FORMULATION OF TABLETS

Table 7.3: Formulation composition for Floating tablets.

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Lansoprazole	15	15	15	15	15	15	15	15	15
Xanthan gum	15	30	45	-	-	-	-	-	-
Guar gum	-	-	-	15	30	45	-	-	-
Sodium Alginate	-	-	-	-	-	-	15	30	45
Sodiumbi Carbonate	8	8	8	8	8	8	8	8	8
Citric acid	8	8	8	8	8	8	8	8	8
Aerosil	5	5	5	5	5	5	5	5	5
Magnesium Stearate	5	5	5	5	5	5	5	5	5

MCC	64	49	34	64	49	34	64	49	34
Total weight	120	120	120	120	120	120	120	120	120

All the quantities were in mg.

7.4.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.

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 wasdetermined from the collective weight. The weight variation test would be a satisfactory method of deter mining the drug content uniformity. Not more than two of the individual weights deviatefrom 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 percentdeviation was calculated using the following formula.

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

Table 7.4: Pharmacopoeial specifications for tablet weight variation.

Average weight of tablet (mg) (I.P)	Average weight of tablet (mg) (U.S.P)	Maximum percentage difference allowed
Less than 80	Less than 130	10
80-250	130-324	7.5
More than	More than 324	5

Hardness

Hardness of tablet is defined as the force applied across the diameter of the tablet in orderto 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 theaverage is calculated and presented with deviation.

Thickness

Tablet thickness is an important characteristic in reproducing appearance. Tablet thicknessis 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. Pre weighed 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, and loss in the weight of tablet is the measure of friability and is expressed in percentageas.

% Friability = [(W1-W2) / W1] × 100Where, W1 = Initial weight of tablets

W2 = Weight of the tablets after testing

Determination of drug content

Both compression-coated tablets of were tested for their drug content. Ten tablets were finely powdered quantities of the powder equivalent to one tablet weight of Lansoprazole were accurately weighed, transferred to a 100 ml volumetric flask containing 50 ml water and were 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. The drug concentration was calculated from the calibration curve.

***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).

***In vitro* drug release studiesDissolution parameters**

Apparatus -- USP-II, Paddle Method

Dissolution Medium -- 0.1 N HCL

RPM -- 50

Sampling intervals (hrs) -- 1,2,3,4,5,6,7,8,10,11,12

Temperature -- 37°c $\pm$ 0.5°c

As the preparation was for floating drug release given through oral route of administration, different receptors fluids are used for evaluation the dissolution profile.

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 ± 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 media and analyzed by spectrophotometricallyat 288 nm using UV-spectrophotometer.

7.5: Application of 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 intozero-order, first order, Higuchi, and Korsmeyer-Peppas release model.

Zero order release rate kinetics

To study the zero–order release kinetics the release rate data are fitted to the following equation.

$F = K_o\ t$

Where, 'F' is the drug release at time't', and 'K_o' is the zero order release rate constant. The plotof % drug release versus time is linear.

First order release rate kinetics: The release rate data are fitted to the following equationLog (100-F) = kt A plot of log cumulative percent of drug remaining to be released vs. time is plotted then it givesfirst order release.

Higuchi release model: To study the Higuchi release kinetics, the release rate data were fitted tothe following equation.

F = k t1/2

Where, 'k' is the Higuchi constant.

In higuchi model, a plot of % drug release versus square root of time is linear.

Korsmeyer and Peppas release model

The mechanism of drug release was evaluated by plotting the log percentage of drug released versus log time according to Korsmeyer- Peppas equation. The exponent 'n' indicates the mechanism of drug release calculated through the slope of the straight Line.

$M_t / M_\infty = K t^n$

Where, M_t / M_∞ is fraction of drug released at time 't', k represents a constant, and 'n' is the diffusional exponent, which characterizes the type of release mechanism during the dissolution process. For non-Fickian release, the value of n falls between 0.5 and 1.0; while in case of Fickian diffusion, n = 0.5; for zero-order release (case I I transport), n=1; and for supercase II transport, n> 1. In this model, a plot of log (M_t / M_∞) versus log (time) is linear.

7.6. Drug – Excipient compatibility studies Fourier Transform Infrared (FTIR) spectroscopy

The compatibility between the pure drug and excipients was detected by FTIR spectra obtained on Bruker FTIR Germany(Alpha T).The solid powder sample directly place on yellow crystal which was made up of ZnSe. The spectra were recorded over the wave number of 4000 cm^{-1} to 550 cm^{-1}.

8. RESULTS AND DISCUSSION

8.1. Analytical Method

a. Determination of absorption maxima

The standard curve is based on the spectrophotometry. The maximum absorption was observedat 288 nm.

b. calibration curve

Graphs of Lansoprazole was taken in 0.1N HCL (pH 1.2)

Table no 8.1: Observations for graph of Lansoprazole in 0.1N HCL.

Copncentration (µg/ml)	Absorbance
0	0
5	0.144
10	0.298
15	0.472
20	0.659
25	0.837

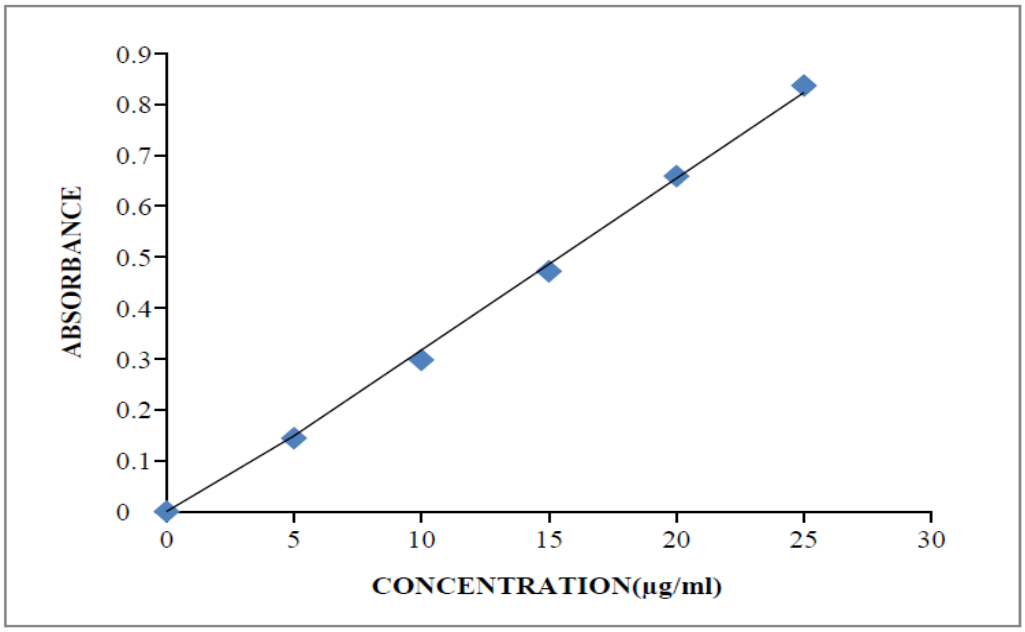


Fig 8.1 Standard graph of Lansoprazole in 0.1N HCL

Standard graph of Lansoprazole was plotted as per the procedure in experimental method and its linearity is shown in Table 8.1 and Fig 8.1. The standard graph of Lansoprazole showed good linearity with R^2 of 0.997, which indicates that it obeys "Beer- Lamberts" law.

8.3.Preformulation parameters of powder blend.

Table 8.2: Pre-formulation parameters of blend.

Formulation Code	Angle of Repose	Bulk density (gm/mL)	Tapped density (gm/mL)	Carr's index (%)	Hausner's Ratio
F1	30.51 ±1.01	0.58 ±0.007	0.71 ±0.011	17.64 ±2.16	1.21 ±0.025
F2	29.36 ±0.58	0.58 ±0.010	0.69±0.0057	16.08 ±0.84	1.26±0.01
F3	35.58 ±0.08	0.58±0.065	0.67 ±0.011	18.15 ±0.74	1.22 ±0.01
F4	34.60 ±0.55	0.56 ±0.007	0.69±0.0095	12.88 ±2.20	1.14 ±0.03
F5	31.30 ±0.92	0.58±0.0075	0.71 ±0.015	20.31 ±2.81	1.25 ±0.041
F6	30.09 ±0.21	0.56 ±0.017	0.70±0.0052	17.95 ±1.64	1.21 ±0.026
F7	30.74 ±0.83	0.56±0.0065	0.64 ±0.012	14.83 ±0.70	1.17 ±0.011
F8	34.20 ±0.74	0.56±0.0080	0.70±0.0072	14.71 ±0.70	1.24 ±0.05
F9	34.05 ±0.93	0.56 ±0.014	0.66±0.0068	15.76 ±1.85	1.18 ±0.02

Tablet powder blend was subjected to various pre-formulation parameters. The angle of repose values indicates that the powder blend has good flow properties. The bulk density of all the formulations was found to be in the range of 0.56 ±0.007 to 0.58 ±0.075 (gm/ml) showing that the powder has good flow properties. The tapped density of all the formulations was found to be in the range of 0.64 ±0.012 to 0.71 ±0.015 showing the powder has good

flow properties. The compressibility index of all the formulations was found to be below 18 which shows that the powder has good flow properties. All the formulations has shown the hausners ratio ranging between 1.14 ±0.03 to 1.26±0.01 indicating the powder has good flow properties.

8.4.Quality Control Parameters For tablets

Tablet quality control tests such as weight variation, hardness, and friability, thickness, Drug content and drug release studies were performed for floating tablets.

8.3. *In vitro* quality control parameters.

Formulation codes	Average Weight (mg)	Hardness (kg/cm^2)	Friability (%loss)	Thickness (mm)	Drug content (%)	Total Floating Time (hrs)	Floating Lag time (sec)
F1	118.48	3.48	0.62	1.52	99.19	10	10
F2	119.61	3.59	0.79	1.78	98.62	12	15
F3	117.32	3.45	0.88	1.47	97.76	12	17
F4	123.73	3.74	0.68	1.65	99.86	12	12
F5	121.55	3.88	0.74	1.77	97.37	11	10
F6	120.92	3.67	0.66	1.55	100.52	12	11
F7	119.44	3.49	0.71	1.64	99.96	12	13
F8	121.30	3.62	0.85	1.72	98.48	12	15
F9	118.22	3.48	0.64	1.59	99.12	12	8

All the parameters for Floating Tablets such as weight variation, friability, hardness, thickness,drug content were found to be within limits.

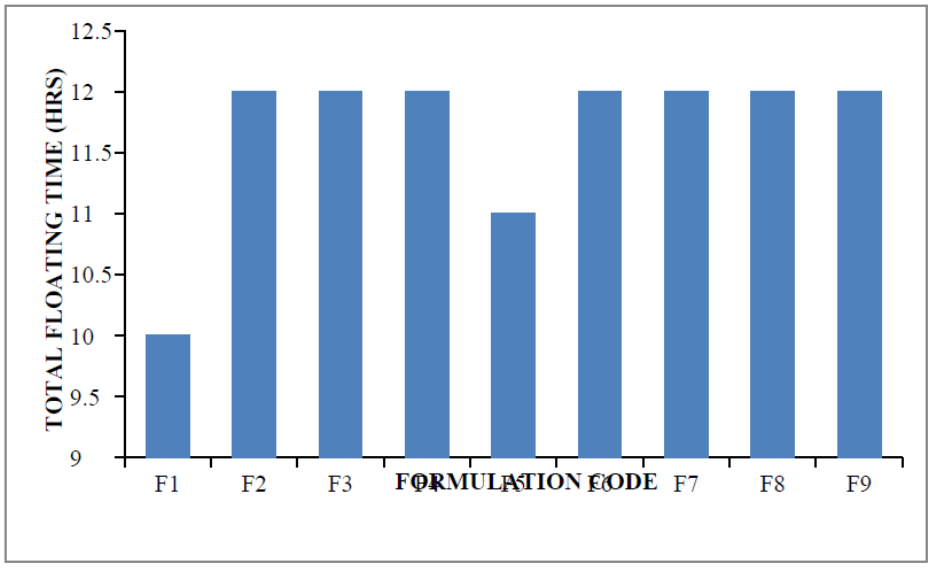


Figure 8.2: Total Floating Time (hrs).

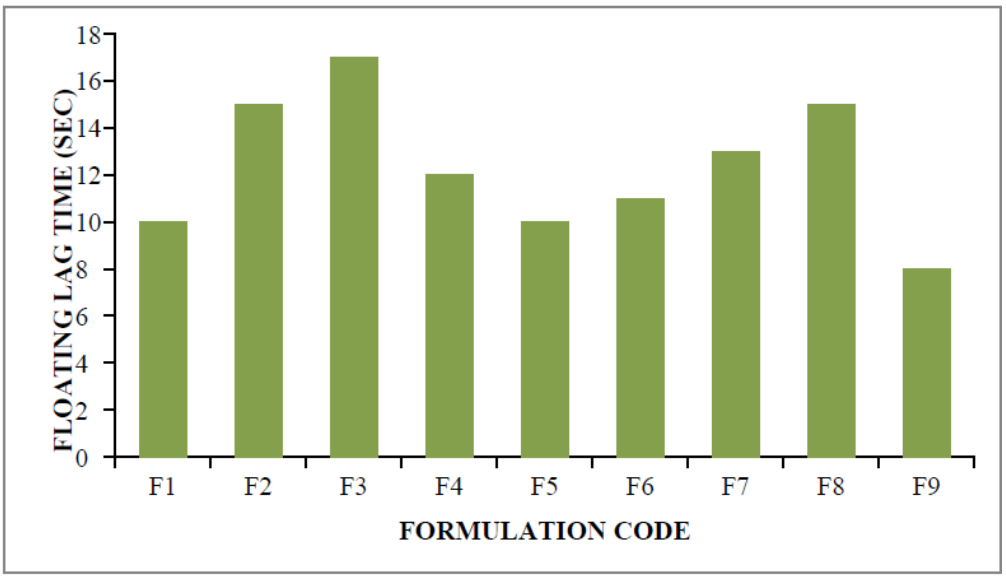


Figure 8.3: Floating Lag time (sec)

8.6. *In vitro* drug release studies

Table no 8.4: Dissolution data of Floating Tablets.

Time (hrs)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
1	14.12	19.38	21.46	26.53	26.77	18.49	21.94	19.33	17.58
2	18.48	21.65	24.78	32.12	33.64	25.66	24.45	21.26	19.86
3	23.64	27.79	32.33	47.88	49.31	33.05	32.72	27.85	22.26
4	26.82	30.96	39.48	58.32	55.22	41.38	40.98	30.14	28.64
5	29.37	33.85	44.24	64.09	61.68	55.16	44.21	33.25	33.02
6	33.64	42.17	57.63	71.66	73.92	62.41	57.58	42.98	46.68
7	37.18	49.65	62.74	77.15	79.17	76.16	62.12	49.21	53.16
8	49.22	55.27	69.41	84.48	86.23	82.71	68.84	55.11	58.01
9	52.59	62.44	74.92	91.32	91.73	88.66	73.22	61.26	63.92
10	63.79	71.58	77.18	92.34	94.52	92.65	77.04	72.81	69.75
11	69.81	77.37	79.82	94.41	94.19	98.16	79.46	77.55	75.91
12	73.28	79.51	82.37	95.44	97.37	99.81	82.17	79.78	78.86

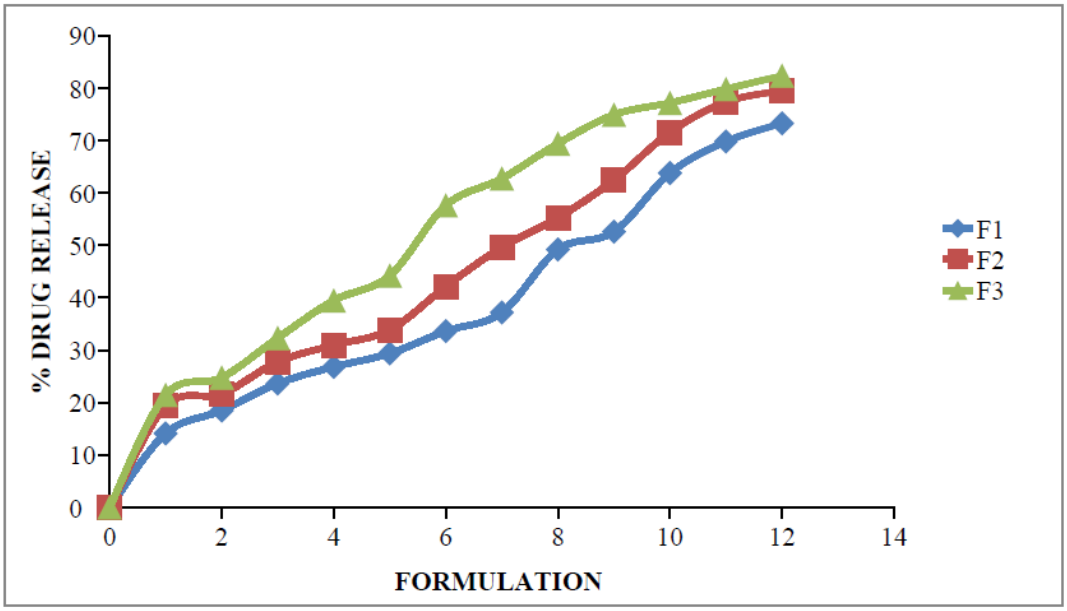


Fig 8.4: Dissolution data of Lansoprazole Floating tablets containing Xanthan gum

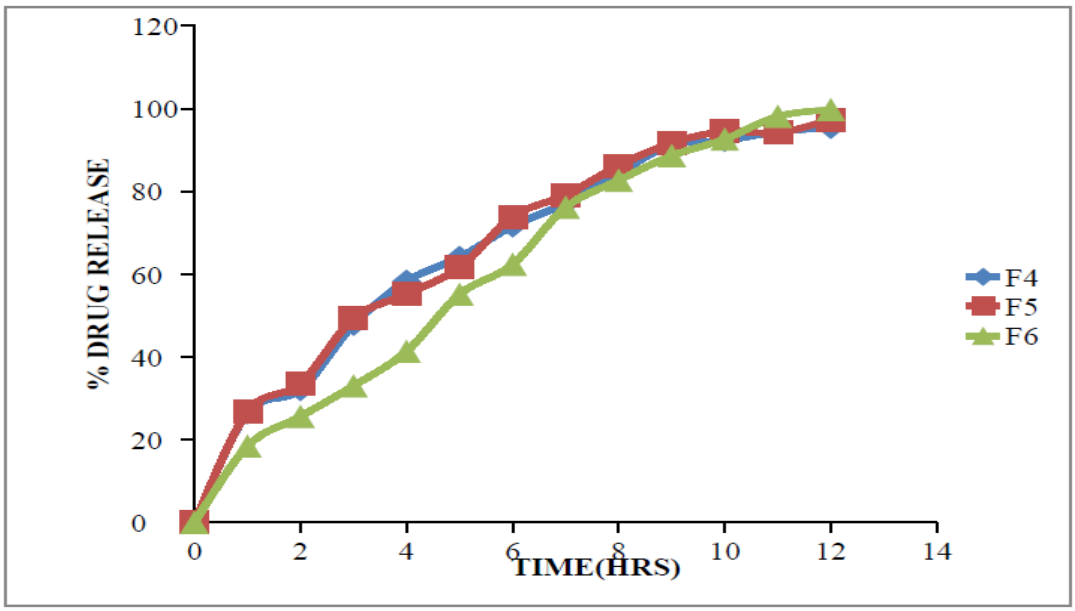


Fig: 8.5:Dissolution data of Lansoprazole Floating tablets containing Guar gum.

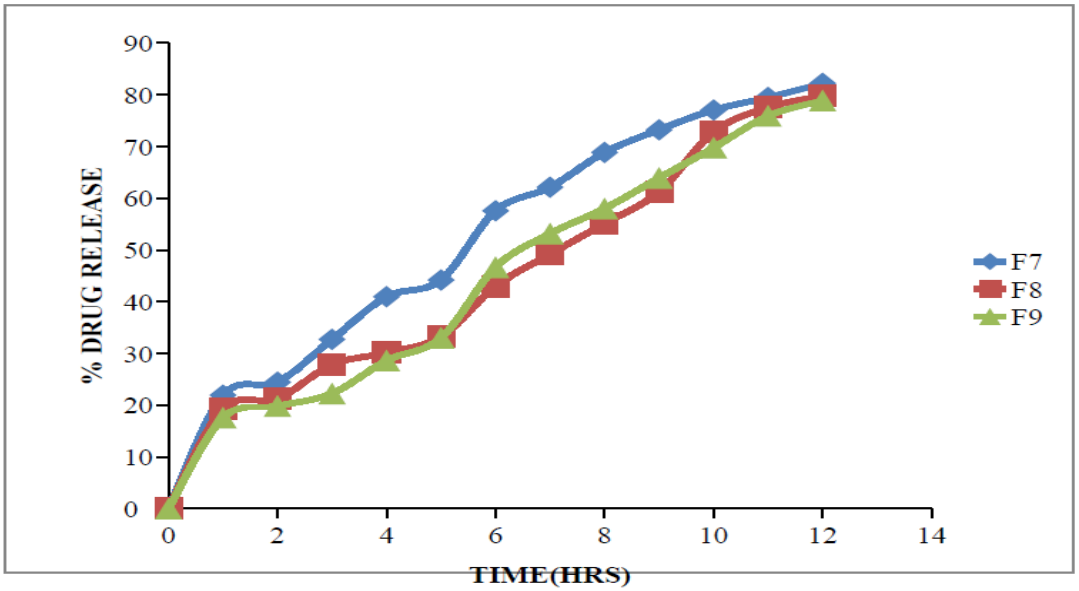


Fig: 8.6: Dissolution data of Lansoprazole Floating tablets containing Sodium Alginate.

Whereas the formulations prepared with higher concentration of Xanthan gum retarded the drug release up to 12 hours. In lower concentrations the polymer was unable to retard the drug release.

Formulations prepared with Guar gum retarded the drug release in the concentration of45 mg (F6 Formulation) showed required release pattern i.e., retarded the drug release up to 12 hours and showed maximum of 99.81 % in 12 hours with good drug release.

The Formulation Containing Sodium Alginate in 15 mg Concentration Showed good retarding nature with required drug release in 12 hours i.e., 82.17 %.

Hence from the above dissolution data it was concluded that F6 formulation was considered as optimised formulation because good drug release (99.81%) in 12 hours.

Application of Release Rate Kinetics to Dissolution Data for optimised formulation.

Table no 8.5 Application kinetics for optimised formulation.

Cumulative (%) Release Q	Time (T)	Root (T)	Log (%) Release	Log (T)	Log (%) Remain	Release Rate (Cumulative % Release/ T)	1/Cum% Release	Peppas Log Q/100	% Drug Remaining	Q01/3	Qt1/3	Q01/3 - Qt1/3
0	0	0			2.000				100	4.642	4.642	0.000
18.49	1	1.000	1.267	0.000	1.911	18.490	0.0541	-0.733	81.51	4.642	4.336	0.306
25.66	2	1.414	1.409	0.301	1.871	12.830	0.0390	-0.591	74.34	4.642	4.205	0.437
33.05	3	1.732	1.519	0.477	1.826	11.017	0.0303	-0.481	66.95	4.642	4.061	0.581
41.38	4	2.000	1.617	0.602	1.768	10.345	0.0242	-0.383	58.62	4.642	3.885	0.757
55.16	5	2.236	1.742	0.699	1.652	11.032	0.0181	-0.258	44.84	4.642	3.553	1.089
62.41	6	2.449	1.795	0.778	1.575	10.402	0.0160	-0.205	37.59	4.642	3.350	1.292
76.16	7	2.646	1.882	0.845	1.377	10.880	0.0131	-0.118	23.84	4.642	2.878	1.764
82.71	8	2.828	1.918	0.903	1.238	10.339	0.0121	-0.082	17.29	4.642	2.586	2.056
88.66	9	3.000	1.948	0.954	1.055	9.851	0.0113	-0.052	11.34	4.642	2.247	2.395
92.65	10	3.162	1.967	1.000	0.866	9.265	0.0108	-0.033	7.35	4.642	1.944	2.697
98.16	11	3.317	1.992	1.041	0.265	8.924	0.0102	-0.008	1.84	4.642	1.225	3.416
99.81	12	3.464	1.999	1.079	-0.721	8.318	0.0100	-0.001	0.19	4.642	0.575	4.067

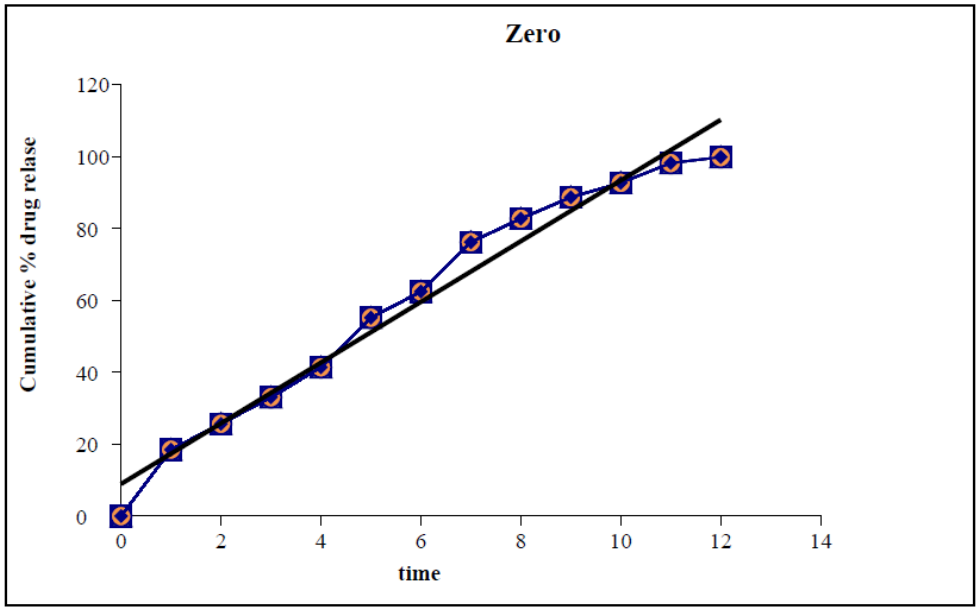


Fig no 8.7: Zero order release kinetics.

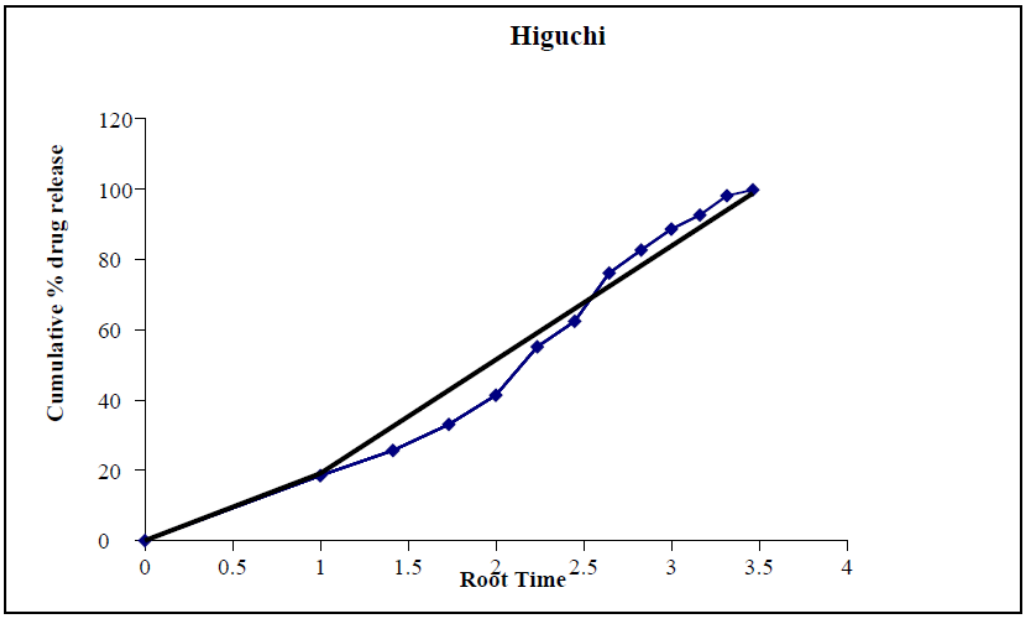


Fig no 8.8: Higuchi release kinetics.

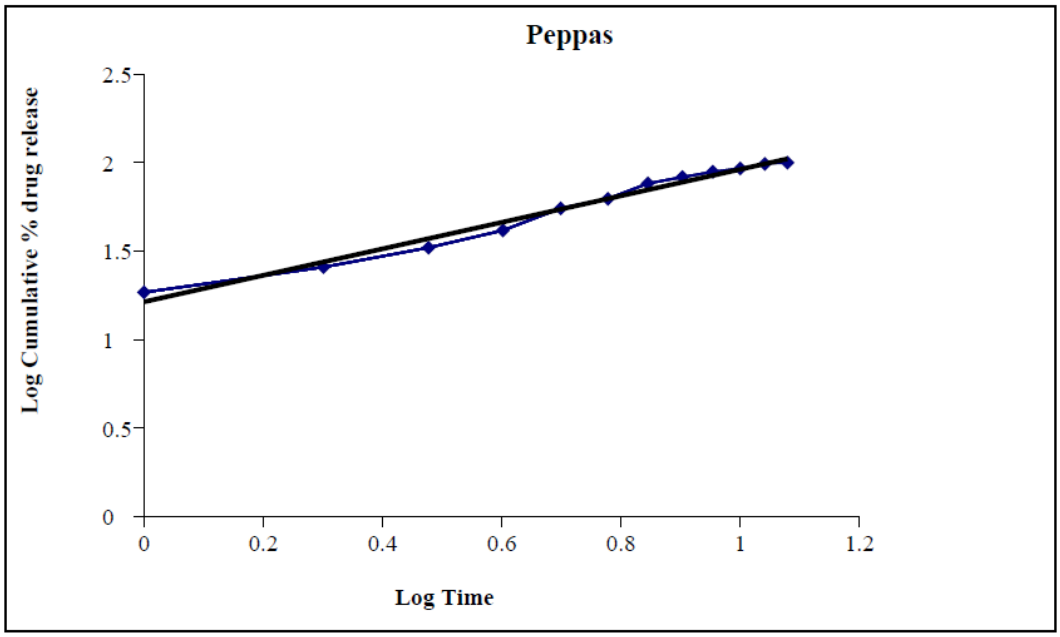


Fig8.9: Kors mayer peppas release kinetics.

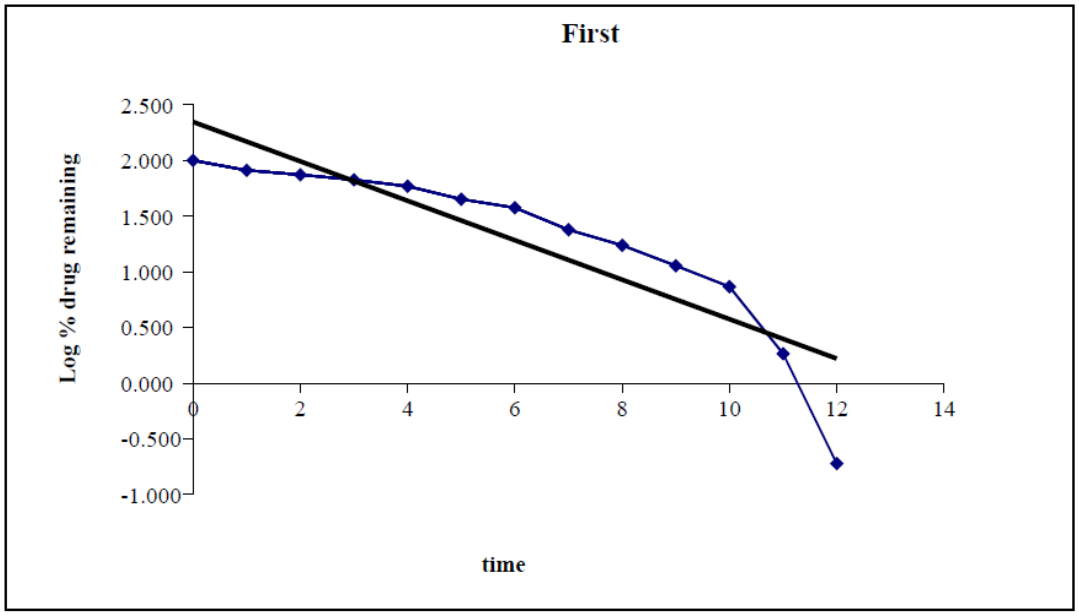


Fig 8.10: First order release kinetics.

Optimised formulation F6 was kept for release kinetic studies. From the above graphs it was evident that the formulation F6 was followed Kors mayer peppas release kinetics mechanism.

8.2. Drug – Excipient compatability studiesFourier Transform-Infrared Spectroscopy

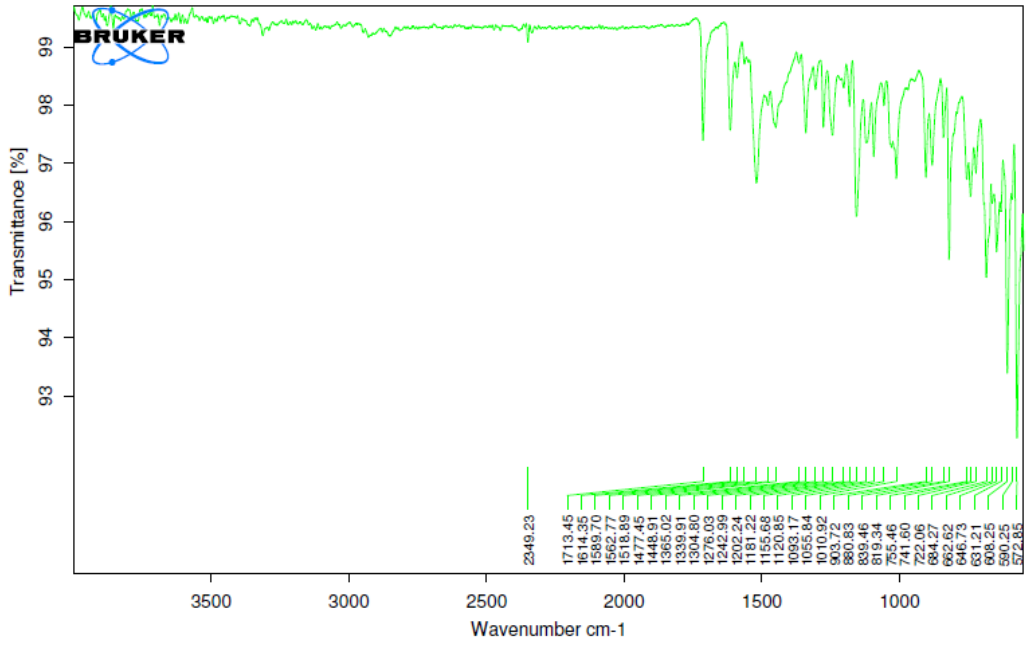


Figure 8.11: FTIR Spectrum of pure drug.

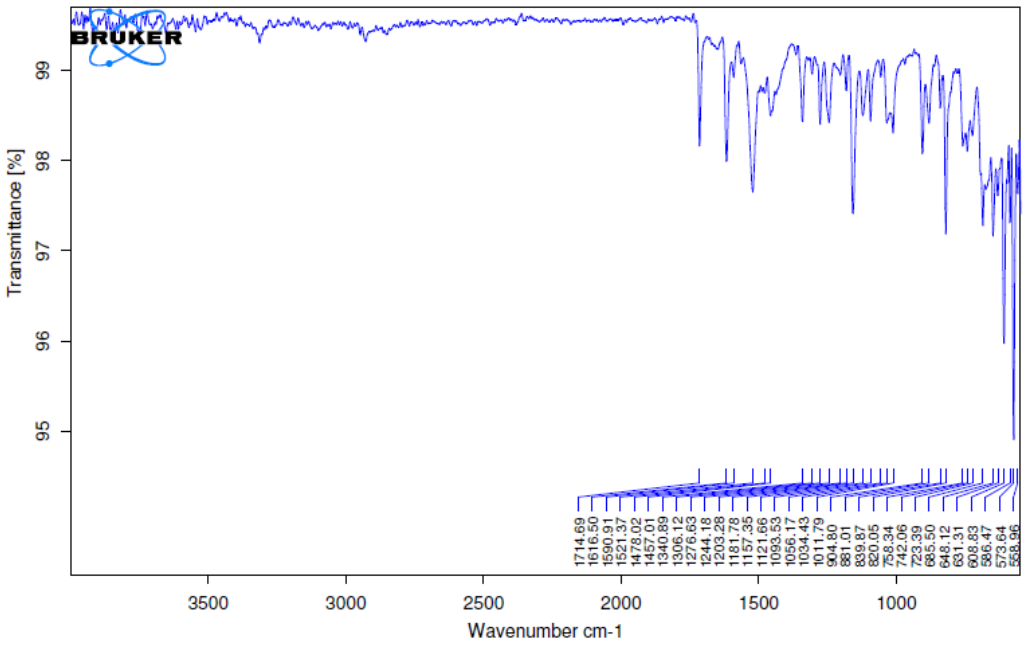


Fig 8.12: FTIR Spectrum of optimised formulation.

There was no disappearance of any characteristics peak in the FTIR spectrum of drug and the polymers used. This shows that there is no chemical interaction between the drug and the polymers used. The presence of peaks at the expected range confirms that the materials taken for the study are genuine and there were no possible interactions.

Lansoprazole are also present in the physical mixture, which indicates that there is no interaction.

CONCLUSION

The objective of the study was to formulate and evaluate Lansoprazole floating tablets. The tablets were formulated using direct compression method using varying quantities of the ingredients like Xanthan gum, Guar gum and Sodium Alginate were used as the polymers and sodium bicarbonate was used as a gas generating agent. The formulated tablets were tested for the parameters such as weight variation, hardness, thickness, friability and drug content and were found to be within the limits. The floating lag time and the floating duration of the tablets are the most important parameters. Hence, diffusion controlled Lansoprazole gastro retentive tablets were formulated and evaluated and formulation F6 was concluded as the best formulation for the manufacture of Lansoprazole gastro retentive tablets which can assure 99 % bioavailability. Floating drug delivery tablets of Lansoprazole were developed to prevent Ulcer disease. The optimized formula F6 showed better sustained drug release and which also had good floating properties.

REFERENCES

1. Leon lachman, herbert a. Liberman, the theory and practice of industrial pharmacy, 293-302.
2. Robinson jr, lee v.h.l, controlled drug delivery: fundamentals and applications, 2nd edn. Marcel dekker, new york, 1978; 24-36.
3. Brahmankar d.m, jaiswal s.b, biopharmaceutics and pharmacokinetics a treatise, 1st ed. Vallabh prakashan; new delhi, 1995; 64-70.
4. Neha Narang. An Updated Review On: Floating Drug Delivery System (Fdds), 2011; 3(1).
5. Chien YW. Rate-control drug delivery systems: controlled release vs. sustained release. Med Prog Techn, 1989; 15: 21-46.
6. Chien YW. Oral drug delivery and delivery system in novel drug delivery Systems, ed,50, Marcel Dekker publication, New York, 1992.
7. Vyas s.p, khar r.k, controlled drug delivery: concepts and advances, 1st ed. Vallabh prakashan, new delhi, 2002; 345-376.
8. Wilson CG, Washington N. The Stomach: its role in oral drug delivery. In: Rubinstein, M.H., (Ed.). Physiological pharmaceutics: biological barriers to drug absorption. Ellis

Harwood, Chechester, 1989; 47-70.

9. Desai S. A Novel Floating Controlled Release Drug Delivery System Based on a Dried Gel Matrix Network [master'sthesis], Jamaica, NY: St John's University, 1984.
10. Davis SS, Stockwell AF, Taylor MJ. The effect of density on the gastric emptying of single- and multiple- unit dosage forms, Pharm Res, 1986; 3: 208- 213.
11. Kaushik Avinash, Dwivedi Abha, Kothari Praween, Govil Abhinav. Floating Drug= Delivery System a Significant Tool for Stomach Specific Release of Cardiovascular Drugs. Int. J. Drug Dev. & Res, October-December 2012; 4(4): 116-129.
12. Soni RP, Patel AV, Patel RB, Patel MR, Patel KR, Patel NM. Gastroretentive Drug Delivery Systems: A Review. International Journal of Pharma World Research 2011; 2(1): 1- 24.
13. Dey D, Pattnaik GD, Sahoo B. An Overview on Gastroretentive Drug delivery systems. PharmaTutor 2011; 1-3.
14. Wilson CG, Washington N. The Stomach: It's Role in Oral Drug Delivery. In: Rubinstein, MH, Editors. Physiological Pharmaceutical: Biological Barriers to Drug Absorption. Chichester, U.K.: Ellis Horwood, 1989; 47-70.
15. Streubel A, Siepmann J, Bodmeier R. Drug Delivery to The Upper Small Intestine Window Using Gastroretentive Technologies. Curr Opin Pharmacol, 2006; 6: 501-508.
16. Shinde AJ, More HN. Gastroretentive Drug Delivery System: An Overview. Pharmainfo.net 2008; 6(1). Available From http://www.pharmainfo.net/reviews/gastroretentiv e-drug-delivery-system-overview
17. Dolas RT, Hosmani A, Bhandari A, Kumar B, Somvanshi S. Novel Sustained Release Gastroretentive Drug Delivery System: A Review. International Journal of Pharma Research and Development, 2011; 2(11): 26-41.
18. Ahuja A, Khar RK, Ali J. Mucoadhesive Drug Delivery Systems. Drug Development & Industrial Pharmacy, 1997; 23(5): 489-515.
19. Sarparanta MP, Bimbo LM, Makila EM, Salonen JJ, Laaksonen PH, Helariutta AM,Linder MB, Hirvonen JT, Laaksonen TJ, Santos HA, Airaksinen AJ. The Mucoadhesive and Gastroretentive Properties of Hydrophobin-Coated Porous Silicon Nanoparticle Oral Drug Delivery Systems. Biomaterials, 2012; 33(11): 3353-3362.
20. A.Geetha, J. Rajendra kumar, CH. Krishna Mohan, V.Sateesh1 & P N Raju. A Review On Floating Drug Delivery Systems. International journal of pharmaceutical research and biomedical analysis | issn: 2278 – 2664 | april-june 2012 Volume 1 | issue 1.

21. Garg.R and Gupta.GD., Progress in controlled gastroretentive delivery systems, Trop J Pharma Res, September 2008; 7(3): 1055-1066.
22. Brahma N. Singh, Kwon H. Kim., Floating drug delivery systems - an approach to oral controlled drug delivery via gastric retention, Journal of Controlled Release, February 2000; 63(3): 235-259.
23. Shukla Shruti et al., A Review On Recent Advancement of Stomach Specific Floating Drug Delivery System, IJPBA, Nov– Dec 2011; 2(6): 1561-1568.
24. Deshpande A.A, Shah N.H, Rhodes C.T, Malick W., Development of a novel controlled-release system for gastric retention. Pharm Res, 1997; 4: 815-819.
25. Bhavana V, Khopade A.J, Jain W.D, Shelly and Jain N.K., Targeted Oral Drug Delivery, Indian drugs, 1996; 33: 365-373.
26. Roop K. Khar, Controlled Drug Delivery, Gastroretentive system 4th edn, 202-203.
27. Khan F.N, Dehghan H.G., Int J Health Res, 2009; 2(1): 23.
28. Deshpande A.A, Shah N.H, Rhodes C.T, Malick W. Pharm Res, 1997; 14: 815-819.
29. Sharma N, Agarwal D, Gupta MK, Khinchi MA Comprehensive Review on Floating Drug Delivery System. International Journal of Research in Pharmaceutical and Biomedical Sciences, 2011; 2(2): 428-441.
30. Sarvesh D Parsekar, Shruti Prabhu, Amitha Shetty, Mohd Azharuddin and AR. Shabaraya. A Brief Review on Floating Bilayer Tablet as a Convenient Gastroretentive Drug Delivery System, Apr-Jun 2014; 3(2).
31. Shrikant M, Shah S and Upadhyay P. Floating Bilayer drug delivery systemAn Unconventional approach in Conventional Form. Am J PharmTech Res, 2012; 2(2): 2249- 87.
32. Dutta P, Sruti J, Patra NC and Rao BME. Floating microspheres: Recent trends and development of gastroretentive floating drug delivery system. Int J Pharm Sci NanoTech, 2011; 4(1): 1296-306.
33. Srujana Katta, Mettu Srikanth Reddy, N. G. Raghavendra Rao. Overview On Floating Drug Delivery System. Am. J. PharmTech Res, 2013; 3(2).
34. Aiswarya Patnaik, Hara Prasad Patnaik. Formulation and Evaluation of Floating Tablet of Pantoprazole Sodium. Volume 9, Issue 1 Version. I (January 2019), PP. 38-43.
35. V. Sarovar Reddy, A. V. Badarinath, K. Gnana Prakash Formulation and Evaluation of Floating Tablets of Ciprofloxacin Hydrochloride. Asian Journal of Pharmaceutics, Apr-Jun 2018; 12(2).
36. Nansri Saha, Pawan Kumar, Satyabrata Bhanja, Soumik Ghosh and Sarita Tiwari

Formulation And Evaluation Of Gastro Retentive Floating Tablets Of Nimodipine. IJRPC, 2018; 8(1): 240-244.

37. Ayesha Salma Habeeb and Shahidulla SM Formulation and in vitro evaluation of captopril floating tablets by using natural polymers. The Pharma Innovation Journal, 2018; 7(8): 82-89.
38. Anas T. Alhamdany, Ali Khidher Abbas Formulation And In Vitro Evaluation Of Amlodipine Gastroretentive Floating Tablets Using A Combination Of Hydrophilic And Hydrophobic Polymers. Int J App Pharm, 2018; 10(6): 126-134.
39. Bharat w. Tekade, Umesh T. Jadhao, Shruti G. Patil, Vijay R. Patil Formulation And In Vitro Evaluation Of Floating Tablets Of Cefpodoxime Proxetil. Int J Curr Pharm Res, 9(6): 18-22.
40. Yerikala Ramesh, Pudi Venkata Prasad, K. Saravanakumar, Vadhireddy Sireesha Formulation And Evaluation Of Floating Drug Delivery Of Cefotaxime Using Raft Forming Approach. Journal of Drug Delivery & Therapeutics, 2017; 7(4): 110-119.
41. Mourya Adarsh, Mrs.P. Haritha Sunil, Praveen Kanna, Sampath.M Design formulation and evaluation of gastroretentive floating tablets of stavudine. Int. J. of Res. in Pharmacology & Pharmacotherapeutics, 2017; 6(1): 93-103.
42. Md. Haider Ali, Mohiuddin Ahmed Bhuiyan, Md. Selim Reza and Samira Karim Formulation and In vitro Evaluation of Oral Floating Tablets of Salbutamol Sulphate: Comparison with Effervescent Tablets. Dhaka Univ. J. Pharm. Sci, 2016; 15(2): 203-208. (December).
43. Ramu Bandameedi and Shanmuga Pandiyan. Formulation and Evaluation of Floating Osmotic Tablets of Nizatidine, November 17, 2015.
44. A. Shiva lakshmaiah, rajesh akki, d. Nagarjuna reddy, V. Vasu naik, a. Anka rao, amjad pasha and sanjay kumar gupta. Formulation and evaluation of hydrodynamically Balanced floating tablets of antidiabetic agent. Acta Chim. Pharm. Indica, 2014; 4(1): 7- 19.
45. L. Kukati, K. Chittimalli, N. B. Shaik. Formulation and Evaluation of Floating Tablets of Cefpodoxime Proxetil. Journal of Scientific Research, 2014; 6(3).