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Floating oral *In-situ* gel: A Review

[1]Bapurao S. Patange, [2] Dr. V. N. Deshmukh
[1]Research Scholar, [2]Professor
[1]Department of Pharmaceutics, Sudhakarrao Naik Institute of Pharmacy, Pusad Dist.Yavatmal.
[1]JSPM's Sudhakarrao Naik Institute of Pharmacy, Pusad Dist. Yavatmal-445204 (MH) India.
[1]bapuraopatange333@gmail.com, [2]go2vilas@rediffmail.com

Abstract-

Gastro-retentive drug delivery System is a Novel Drug Delivery which is mainly Comprised of Floating, Mucoadhesive, Swellable and High Density system. Floating Drug delivery system meants for gastic retention, float on the surface of the gastric fluids, due to their low density and produce prolonged effect by showing release, while being buoyant on gatric fluid surface.In-situ gels are the solutions or suspensions that undergo gelation after reaching the particular site due to contact with body fluids or physicochemical changes.

Conventional oral dosage forms having low bioavailability due to rapid gastric transition from stomach and requires more dosing frequencies, the floating oral in situ gel have a ability to overcome these problems. Floating oral In-Situ gelling System having controlled released and site specific drug delivery hence it has a great interest to researchers in pharmaceuticals to improve the therapeutic advantages.

In these review we discuss the Gastro-retentive drug delivery system specially Floating oral in-Situ gelling system with Natural and Synthetic polymers, Approaches of formulation and its brief Evaluation Parameters that having great advantages in Pharmaceutical formulations.

Keywords-Floating drug delivery,In-situ gel, buoyant, swelling polymers, cross-linking gelation, FTIR etc.

Introduction-

Floating Drug Delivery System (FDDS) is one of the novel system of drug delivery In-situ gelling system is a new trend in FDDS. In-situ gelling system have its application in different routes of administration like oral, nasal, ophthalmic, peroral, rectal, vaginal and also Parenteral route. In situ forming polymeric drug delivery

systems has many advantages such as ease of administration, increased local bioavailability, reduced dose frequency, improved patient compliance and has less complex method of production and so is cost effective.

Gastroretentive FDDS have bulk density lower than gastric fluid and hence remain buoyant in stomach without affecting the gastric emptying rate for a long period of time. When the gel so formed float on gastric fluid the drug get released slowly at desired rate from the floating gel. A gel is a soft, stable, or solid-like material which consists of at least two components, one of them being a liquid, present in substantial quantity [1]

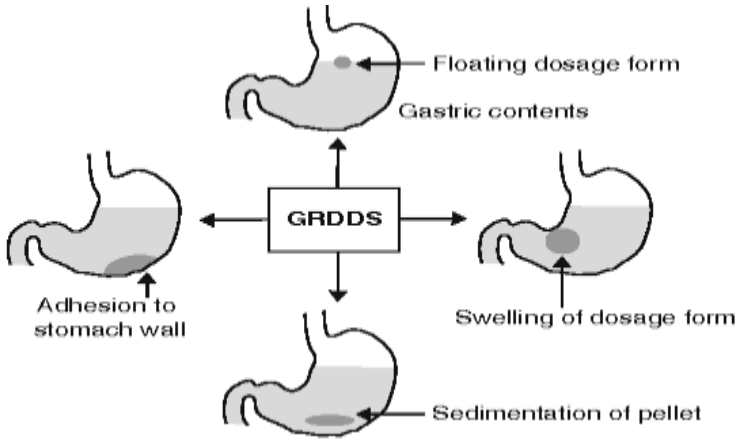

Fig.1: Classifications of GRDDS

Floating Drug Delivery System:-

Floating drug delivery systems was first described by Davis in 1968. These are low-density systems that have sufficient buoyancy to float over the gastric contents and remain in the stomach for a prolonged period and one of the important approaches to achieve gastric retention and to obtain sufficient drug bioavailability. This system is desirable for drugs with low absorption window in the stomach or in the upper small intestine. FDDS having a bulk density lower than gastric fluids and thus, that remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time.

Advantages [2]

1) To decrease the wastage of drug
2) To ease of administration
3) It administered to unconscious and old patients
4) It helps to extended or prolonged release of drugs
5) It allows more patient comfort and compliance
6) Due to the low dose, there will be no drug accumulation and minimize the drug toxicity
7) It offers more bio-availability

8) By using natural polymers, provides biocompatibility and biodegradation.
9) By using synthetic polymers usually well-defined that can be modified to yield tolerable degradability and functionality.
10) To Facilitate drug targeting primarily through mucus membranes, for non-invasive drug administration
11) It offers a vital stealth characteristic *in vivo*, owing to its hydrophilicity, which increases the *in vivo* circulation time of the delivery device
12) It exhibits bio-adhesiveness to facilitate drug targeting, primarily through mucus membranes, for non-invasive drug administration
13) To reduce the systemic absorption of drugs drained through the nasolacrimal duct

Disadvantages

1) Requires a high level of fluids
2) The solution form of the drug is more susceptible to degradation
3) Due to chemical degradation, there is a chance of stability problems
4) Eating and drinking restricted for a few hours after placing the drug
5) Only small doses administered
6) Due to low mechanical strength, it may result in premature dissolution
7) Particularly for hydrophobic drugs, the quantity and homogeneity of drug loading into hydrogels may be limited.

Comparison between Conventional and Floating Drug Delivery System:-

Conventional Drug Delivery System	Gastro Retentive Drug Delivery System
More Side Effect	No Risk found
Patient compliance is Less	Improves patient compliance
Not Appropriate for delivery of drugs with narrow absorption window in small intestine region	Appropriate for delivery of drugs with narrow absorption window in small intestine region
Not beneficial for drugs exhibit local action in stomach and degrade in the colon having rapid absorption through GIT	Beneficial for drugs exhibit local action in stomach and degrade in the colon having rapid absorption through GIT
Less gastric retention time	Improves gastric retention time

Polymers in Floating in situ Gel-[3]

Polymers are generally employed in floating drug delivery systems so as to target the delivery of drug to a specific region in the gastrointestinal tract i.e. stomach. Both synthetic and natural polymers have been studied extensively in the design of drug delivery systems. In spite of the advent of many synthetic polymers, use of natural polymeric materials has gained lot of importance during the last two decades in drug delivery arena. Incorporation of natural polymers in various drug delivery systems looks to be an active avenue of research and development due to obvious reasons of compatibility, inexpensive and ready availability.

Natural polymers used in *In-situ* gel Preparation –

1) Xanthan Gum

Xanthan gum is a high molecular weight extracellular polysaccharide produced by pure culture aerobic fermentation of carbohydrate with Xanthomonas *campestris* bacteria.[3] Xanthan is a long chained polysaccharide with large number of trisaccharide side chains. The main chain consists of b-(1,4)-linked D-glucose units. The side chains are composed of two mannose units and one glucoronic acid unit. This gum develops a weak structure in water, which creates high viscosity solutions at low concentration.Viscosity remains fairly constant from 0°C to 100°C.[4]

2) Gellan Gum

Gellan gum is an anionic, high molecular weight, deacetylated extracellular linear polysaccharide comprising glucuronic acid, rhamnose and glucose. It is produced as a fermentation product by a pure culture of Pseudomonaselodea. Gellan gum, also commercially known as Phytagel or Gelrite.It is capable of gelation in the presence of mono- and divalent ions. It is available in two forms (high or low acyl content). This gum has an out standing flavor release, high gel strength, an excellent stability, process flexibility, high clarity, good film former and thermally reversible gel characteristics.[6,7]

Rajnikanth et al prepared and evaluated gellan based floating beads of acetohydroxamic acid by ionotropic gelation method. Prepared beads showed good antimicrobial activity as potent urease inhibitors. They concluded that an oral dosage form of floating gellan beads containing this drug may form a useful stomach site specific drug delivery system for the treatment of H. pylori infection.[8]

3) Karaya Gum

Karaya gum is a vegetable gum produced as an exudate by trees of the genus *Sterculia*. Chemically, gum karaya is an acid polysaccharide composed of the sugars galactose, rhamnose, and galacturonic acid. Gum is least soluble of commercial plant exudates, but it absorbs water rapidly and swells to form viscous colloidal solutions even at low concentrations (1%). Swelling behavior of karaya gum is dependent upon the presence of acetyl groups in its structure.

Eaga et al formulated and evaluated sustained release floating matrix tablets of atenolol and S-atenolol using natural hydrophilic polymers such as guar gum, xanthan gum and karaya gum. Results reveal that each gum has different abilities to hydrate and swell on contact with water. It has also been concluded that gums are capable of producing zero order drug release by diffusion mechanism.[8]

4) Psyllium Husk [8]

Psyllium husk obtained from dried seed coats of *Plantago ovate* is swellable, biocompatible, inexpensive, inert, environment friendly and easily available polymeric substance. The seed contains 5-10% lipids with unsaturated fatty acids, sterols, proteins (15-18%), traces of cyclopentanopyridine-type alkaloids, aucubin and carbohydrates-planteose, a trisaccharide, and10-12% mucilage of the heteroxylan type.73Psyllium husk has also release retardant properties. the characteristics reveal a psyllium husk is most likely to serve as a viable means for gastroretentive drug delivery system.

Chavan Patil et al developed sustained release floating tablets of ofloxacin using various combinations of psyllium husk, HPMC K100M and crospovidone. Formulations were also evaluated for buoyancy lag time, duration of buoyancy, dimensional stability, drug content and in vitro drug release profile.[9]

5) Pectin: [10]

These are plant origin anionic polysaccharides isolated from the cell wall of most plants and basically consist of -(1-4)-D-galacturonic acid residues. Pectin undergoes gel formation in presence of divalent ions (e.g. Ca) which causes cross linking of the galacturonic acid units (ionic cross linking) and also in the presence of the H ions (pH dependent gelling).

6) Xyloglucan [11]

It is a plant based polysaccharide obtained from seeds of tamarind. Chemically, this polysaccharide composed of a chain of (1-4)- -D-glucan having (1-6)- -D xylose units as branches which have partial (1-2)- -D-galactoxylose substitution.

Xyloglucan, itself, does not undergo gel formation but dilute solutions partly degraded by galactosidase exhibit gelling properties on heating (temperature dependent gel formation).[9]

7) Chitosan [3]

Chitosan is a natural and versatile polymer obtained by alkaline deacetylation of chitin. It has favorable biological properties such as non-toxicity, biocompatiblity, and biodegradability. Being a bioadhesive polymer and having antibacterial activity, this polymer is a excellent agent for site specific drug delivery.

Chitosan molecule is a copolymer of N-acetyl-D-glucosamine and D-glucosamineChitosan is a high molecular weight polycationic weak base with pKa value of the D-glucosamine residue of about 6.2-7.0 and, therefore, is insoluble at neutral and alkaline pH values. By increasing the chitosan membrane's thickness, the

release rate of the drug decreased. Both chitosan granules and chitosan-laminated preparations could be helpful in developing drug delivery systems that will reduce the effect of gastrointestinal transit time.

Synthetic polymers used in *In-Situ* Gel-

The system was based on three polymers having different functions such as GG, polymer capable of gelling in presence of ions, MC, polymer characterized by a gelation temperature close to 50 ◦C, and HPC, polymer capable to interact with mucin/mucosa. The three polymers synergistically act to obtain the formation of a protective gel layer with a prolonged permanence on the mucosa.[12]

1) Alginic Acid[13]

Alginic acid is a linear block copolymer polysaccharide consisting of β-D-mannuronic acid (M) and α-L-guluronic acid (G) residues joined by 1,4-glycosidic linkage. Dilute aqueous solutions of alginates form firm gels on the addition of di- and trivalent metal ions by a co-operative process involving consecutive guluronic residues in the G blocks of the alginate chain. This property has been widely exploited for the fabrication of vehicles for the sustained delivery of bioactive molecules, usually as matrix devices.

2) Hydroxypropyl Methyl Cellulose (HPMC)

Hydroxypropyl Methyl Cellulose (HPMC) as a partly O-methylated (OCH3) and O-(2-hydroxypropylated) (OCH2CH (OH) CH3) cellulose conforming to the limits for the various types of HPMC as in Fig. 18. It is available in several grades that vary in viscosity (50-100000 cps), and Molecular weight is approximately 10000-1500000.[13]

It is widely used in oral, ophthalmic, nasal, and topical pharmaceutical formulations as coating agent, controlled-release agent, dispersing agent, dissolution enhancer, extended-release agent, film forming agent, modified-release agent, release modifying agent, solubilizing agent, stabilizing agent, sustained-release agent, thickening agent, and viscosity-increasing agent.[14]

3) N-Propylacrylamide Copolymers

Poly (N-isopropylacrylamide) (pNiPAAm) is a non-biodegradable polymer with a LCST, 32ºC in water, and cross-linked gels of this material collapse around this temperature.

Recent developments on pNiPAAm based hydrogels include their use for drug delivery cell encapsulation and delivery and cell culture surfaces.[15]

4) Carbopol

It is a well-known pH-dependent, which stays in solution form at acidic pH but forms a low viscosity gel at alkaline pH. In combination with HPMC, impart the viscosity of carbopol solution while reducing the acidity of the solution [16]

5) Poloxamer

These polymers are ABA-type triblock copolymers composed of PEO (A) and PPO units (B). The poloxamer series covers a range of liquids, pastes, and solids, with molecular weights and ethylene oxide-propylene oxide weight ratios varying from 1100 to 14,000 and 1:9 to 8:2, respectively. Concentrated aqueous solutions of poloxamer form thermoreversible gels.

Poloxamer 407 (Pluronics F127) was found to gel at a concentration of 20 %wt at 25oC, which is less than that of the other members of the poloxamer series. At room temperature (25oC), the solution behaves as a mobile viscous liquid, which is transformed into a semi-solid transparent gel at body temperature (37oC).

Approaches to Designing Floating Oral in-situ Gel System:

1) Physically Induced in-situ Gel Systems: [17]

A. Swelling:

In-situ gel formation occurs when polymeric lipid absorbs water from the surrounding environment and expands to give the desired space.

B. Diffusion:

In this method the diffusion of solvent from polymer solution into surrounding tissue and results in precipitation or solidification of the polymer matrix.

2) Chemically Induced in-situ Gel Systems[18]:

A. Ionic Cross-linking:

Many ion sensitive polysaccharides such as sodium alginate, iota carrageenan, gellan gum(Gelrite®), pectin undergo a phase transition in the presence of various ions such as K+ , Ca2+, Mg2+, Na+ . The formation of in-situ gel involves administration of solutions, once administered they form a gel inside the stomach under certain conditions involving the use of a gelling agent which can form a system that contains the dispersed drug and other excipients.

The gelling of this system is achieved by using polymer solutions such as sodium alginate triggered by ionic complexation that contains divalent-ions complexed with Na-citrate which breakdown in the acidic environment of the stomach to release free divalent ions (Ca2+) due to change in pH. The free Ca2+ ions get entrapped in polymeric chains thereby causing cross-linking of polymer chains to form matrix structure causes the in-situ gelation of the orally administered solution

B. Enzymatic Cross-Linking:

In-situ gel formation catalyzed by natural enzymes. For example, cationic pH-sensitive polymers containing immobilized insulin and glucose oxidase can swell in response to blood glucose level releasing the entrapped insulin. Thus, adjusting the amount of enzyme controls the rate of gel formation, which allows the mixtures to be injected before gel formation.

In situ formation induce by natural enzymes and that are not been investigated widely but appear to have some advantages over chemical and photochemical methods. For example, an enzymatic process handles efficacy under physiologic conditions and no need for possibly destructive chemicals such as monomers and initiators.

Hydrogels are used in intelligent stimuli-responsive delivery systems that can release insulin have been investigated. Modify the amount of enzyme also maintain a suitable mechanism for controlling the rate of gel formation, which confess the mixtures to be injected before gel formation [19]

C. Photo-Polymerization:

A solution of monomers such as acrylate or other polymerizable functional groups and initiator can be injected into tissue site and the application of electromagnetic radiation used to form gel designed to be readily degraded by chemical or enzymatic processes or can be designed for long term persistence in-vivo. Typically long wavelength ultraviolet and visible wavelengths are used, while short wavelength ultraviolet is not used because it has limited penetration of tissue and biologically harmful.

The polymers which undergo dissociation by polymerisable functional group in the presence of photo initiator like acrylate or similar monomers and macromers that are typically long wavelength ultraviolet and visible wavelengths are used. Short wavelength ultraviolet are not used often because they are limited penetration of tissue and biologically harmful. In this method, ketone, such as 2,2 dimethoxy-2-phenyl acetophenone, is used as the initiator for ultraviolet photo- polymerization. Camphorquinone and ethyl eosin initiators are used in visible light systems.[19]

3) In-situ Gel Formation based on Physiological Stimuli:

A. Temperature Dependent in-situ Gelling:

Temperature-induced in situ gelling systems also known as thermally triggered systems. In these systems, no external heat other than body temperature is required to cause gelation. These are the most widely used systems. These hydrogels are liquid at room temperature (20ºC - 25ºC) and undergo gelation when contact body fluids (35ºC-37ºC), due to an increase in temperature.[19]

Temperature induced or thermal sensitive in situ gel system classified into three types –[2]

i. Negatively thermo-sensitive type:

e. g., poly-N-isopropyl acrylamide (PNIPAAm)

ii. Positively thermo-sensitive type,

e. g., polyacrylic acid (PAA), poly (acrylamide-co-butyl methacrylate)

iii. Thermally reversibly type; e. g. poloxamer, pluronic (poloxamer), tetronics.

B) pH triggered systems in this approach,

pH-responsive or pH-sensitive polymers to be used to form a gel. All pH-sensitive polymers contain acidic or alkaline ionizable functional groups and that either loose or let accept protons in comeback to change in pH.

In pH sensitive polymers includes pendant acidic or basic groups that may accept or release protons in counter to changes in environmental pH. The large number polymers of ionizable groups are known as poly electrolytes. The poly electrolytes are present in the formulation causes increase in external pH that leads to swelling of hydrogel that forms in situ gel. Some suitable polymers for this approach those polymers having anionic groups. Some are cellulose acetate phthalate (CAP), carbomer and its derivatives, polyethylene glycol (PEG), pseudo latexes and poly methacrilic acid (PMC) etc.[19]

MECHANISM OF *IN-SITU*GELATION[19]

These are aqueous liquid solutions before administration, but gel under physiological conditions. Several possible mechanisms lead to in-situ gel formation are: Ionic cross linkage, pH change and temperature modulation. Polymer solutions of gellan, pectin & sodium alginate, etc. contain divalent ions complexed with sodium citrate that are breakdown in the acidic environment of stomach to release free divalent ions (Ca+2) causes the in-situ gelation of orally administered solution. It involves the formation of double helical junction zones by aggregation of double helical segments to form dimensional network by complexation with cations and hydrogen bonding with water.

While the system is floating on the stomach, the drug is released slowly at the desired rate from the system. After release of drug, the residual system is emptied from the stomach besides a minimal gastric content needed to allow the proper achievement of the buoyancyretention principle, a minimal level of floating force (F) is also required to keep the dosage form reliably buoyant on the surface of the meal.

EVALUATION OF FLOATING ORAL *IN-SITU*GEL:

A. Physical appearance and pH:

In situ solutions should be clear and free of any particulate matter. Time required for solution to convert in to gel in buffer pH 1.2 is measured and consistency of the gel formed is checked visually.[10]

Clarity of solution is one of the most important characteristic of preparation. The clarity of solutions was determined by visual inspection under black and white background. The pH was measured by using a calibrated digital pH meter at 25°C. [20]

B. Viscosity :

Viscosity of all the formulations was determined using a Brookfield digital viscometer by 1°C before±using spindle number 2 at 50 rpm. The sample temperature was controlled at 25 each measurements.[10]Viscosity of solution is determined before and after gelling by using Brookfield viscometer or cone and plate viscometer at suitable temperature (25±1 C), using 1or 2ml of sample aliquots.[20]

The formulation should have an optimum viscosity that allow easy of swallowing as a liquid, which then undergoes a rapid sol-gel transition due to ionic interaction show the shear dependency of the viscosity which reduced upon application of the shear on the solutions, all polymer concentrations showed evidence of shearthinning behavior, the effect being more pronounced at higher concentrations. This shear thinning behavior provides an advantage for the administration process,shaking of the formulation increases its fluidity pourability.The observed increase in viscosity with increase in concentration has been noted previously for Gellan and was attributed to a consequence of increasing chain interaction with polymer concentration. Increasing the Calcium Carbonate content in the formulation simultaneously increased the viscosity at all polymer concentrations studied. Since the Calcium Carbonate is present in the formulations as insoluble dispersion, an increase in its concentration proportionally increased the number of particles dispersed, thus contributing to increased viscosity.[21]

C. *In-Vitro* Gelation Study :

To evaluate in vitro gelling capacity of gel forming solution, colored solution of the formulation is prepared and in a test tube 15ml gelation medium (0.1N HCl, pH 1.2) is taken. After that, 1ml of colored formulation is added. As, the solution comes in contact with gelation medium a Stiff gel is produced. A Gelling capacity is Determined on the basis of Stiffness and time period for which gel remains constant. [10]

Evaluation for gelling capacity canalso measure by visualization method. In this method, 5ml of 0.1 N HCL was taken in glass tube and maintained at 37°C±1°C. Various parameters like the time taken for in situ gel formation, visual stiffness of gel and the duration of gel remains intact was observed.[20]

D. *In vitro* floating study:

The Floating ability of the gel is determined in 500ml simulated dissolution apparatus (type II). After that, 10ml of prepared formulation is introduced in the dissolution vessel. Time taken by formulation to float (floating lag time) and duration for which the formulation floats constantly on the surface (floating time) is noted.[10]

The time taken for the formula to emerge to the surface of the medium, and the duration of floating (DOF), the time the formula constantly floated on the medium surface for each formula.

The in vitro gelling capacity was graded in three categories based on FLT and DOF, as follows:

a) Low gelling capacity (+): FLT (immediate gelation) and DOF < 12 h
b) Intermediate gelling capacity (++): FLT (immediate gelation) and 24 h > DOF > 12 h
c) High gelling capacity (+++): FLT (immediate gelation) and DOF > 24 h

This study was performed by placing an accurately weighed sample (1 g) of each formula in a test tube containing 10 mL of the simulated gastric fluid USP without pepsin enzyme (constituents: 2 g NaCl and 7 mL HCl in D.W. to make 1 L), and samples were then observed for their floating behavior.[22]

E. In vitro drug release:

In vitro drug release is determined using USP dissolution apparatus (type II) at 50 rpm in 900ml, 0.1N HCl, pH 1.2 at 37 C. 10ml formulation is taken in a Petri dish and kept in dissolution vessel. Then dissolution medium is introduced in the dissolution vessel without any disturbance. Suitable sample is drawn at each predefined interval and replenished with fresh medium. Dissolution study should be carried out for at least 8 hours.[10]

The in situ gel preparations was determined as described by Zatz and Woodford (1987) with some modification using USP dissolution test apparatus (USP type II) with a paddle stirrer at 50 rpm. This speed was slow enough to avoid the breaking of gelled formulation and was maintaining with the mild agitation conditions believed to exist in vivo. The dissolution medium used was 900 ml of 0.1 N HCl (pH 1.2), and temperature was maintained at 37°C. 5 ml of formulation was drawn up into the dissolution vessel containing dissolution medium with help of pipette without much disturbance. The 5ml of sample from dissolution medium was withdrawn at different time interval up to 8 hrs and sync condition was maintained. The samples were diluted and analyzed under UV spectrophotometer at λmax of 287nm.[20,23,24]

F. Stability studies :

The room temperature storage condition was 25±5˚C and 65% RH and the conditions for accelerated stability studies was 40±2˚C temperature at Relative Humidity of 75±5%. Stability is to be tested for 30 days.[20]

G. Polymer Drug Interaction-

The Polymer-Drug Interaction Can be evaluated by FTIR Instrument.

a) Fourier Transform Infrared Analysis-

Fourier transform infrared spectroscopy is a technique mostly used to identify organic,polymeric, and some inorganic materials as well as for functional group determination.

Drug-excipients interactions play a vital role in the release of drug from formulation. Fourier transform infrared spectroscopy has been used to study the physical and chemical interactions between drug and the excipients used. The pure amoxicillin and its mixture with sodium alginate and HPMC K100 were mixed separately with IR grade KBr and were scanned over a range of 400–4500 cm−1 using FTIR instrument (FTIR1700, Shimadzu, Kyoto, Japan). The drug exhibits peak due to ketonic, primary amine, secondary amine, and hydroxyl (broad) group. [25]

b) Differential scanning calorimetry (DSC)

DSC results provide both qualitative and quantitative information about the physicochemical state of the drug present in formulation.

The DSC analysis of the pure drug and the drug-loaded in-situ gels was performed by using an automatic thermal analyzer system to evaluate the drugpolymer interactions (17). The analysis was performed at a rate of 20^{o} C min from 50^{o} C to 300^{o} C under a nitrogen flow of 25 mL/min.[26]

H. Swelling index:-

The gel swelling index of the selected formulation is determined by a simple method. In this study, an in-situ gel formed in 40 ml of0.1N HCl (pH 1.2) was used. Separate the 0.1N HCl gel fraction from each formulation, and remove the excess HCl solution with paper towels. Weigh the initial weight of the gel, add 50 ml of distilled water to the gel, pour out the water after 12 hours, record the weight of the gel, calculate and report the weight difference [25]

Conclusion-

The formulation and evaluation of floating oral In-Situ gelling System provides various advantages over conventional oral dosage forms. The use of Natural and synthetic polymers for in situ gel formulation can make excellent drug delivery system. By understanding floating and gel forming behavior of polymers we can look forward to improve the gastric retention and hence bioavailability of various drugs.

References:

1. R. Bashir, A. Majeed, T. Ali,S. Farooq, N. Ahmad Khan, Floating Oral In-situ Gel: A Review. JDDT, 2019; 9(2): pp.442.

2. B. Padmasri, R. Nagarju, D. Prasanth. a comprehensive review on in situ gels: Int J App Pharm, Vol 12,2020: pp.24-25.

3. R. Pahwa, S. Bhagwan, V. Kumar, K. Kohli, .Role of Natural Polymers in the Development of Floating Drug Delivery Systems. Journal of Pharmacy Research 2010, 3(6): pp. 1312-1318.

4. C.Kapadia, V.Mane, Raft-forming agents: Antireflux formulations, Drug Dev. Ind. Pharm., 33(12), 2007, pp. 1350-1361.

5. Vendruscolo CW, Andreazza IF, Ganter JLMS, Ferrero C, Bresolin TMB, Xanthan and galactomannan (from M. scabrella) matrix tablets for oral controlled delivery of theophylline, Int. J. Pharm., 296(1-2), 2005, 1-11.

6. K. Bhardwaj, Kanwar M, Lal R, Gupta A. Natural gums and modified natural gums as sustained release carriers. Drug Dev. Ind. Pharm., 26(10). pp. 1025-1038.

7. Gellan gum, http://en.wikipedia.org/wiki/Gellan_gum accessed on 20 Jan. 2010

8. PS Rajinikanth, B.Mishra, Preparation and in vitro characterization of gellan based floating beads of acetohydroxamic acid for eradication of Helicobacter pylori, Acta Pharm.57(4), 2007, pp.413-427.

9. M.Chavanpatil , Jain P, S. Chaudhari, Shear R, Vavia P, Development of sustained release gastroretentive drug delivery system for ofloxacin: In vitro and in vivo evaluation, Int. J. Pharm., 304(1-2), 2005, pp. 178-184.

10. L. Bharadwaj, P. Sharma, and RishabhaM, A Short Review on Gastro Retentive Formulations for Stomach Specific Drug Delivery: Special Emphasis on Floating In situ Gel Systems, African J. Basic & Appl. Sci., 3 (6): pp. 305-306.

11. H Rathod., V. Patel and M. Modasia, In situ gel as a novel approach of gastroretentive drug delivery, International Journal of Pharmacy and Life Sciences, 1(8): pp. 440-447.

12. V Barbara, R Silvia, Giuseppina S, Maria Cristina B , Carla M.C, and Franca F, Recent Advances in the Development of In Situ Gelling Drug Delivery Systems for Non-Parenteral Administration Routes, Pharmaceutics 2020,pp.15-16.

13. RG Shaikh, S. Shah, K. Patel, B. Patel, B. Patel, A Review on Polymers Used in In-Situ Gel Drug Delivery Systems, IJPRS V-1, I-2, 2012, pp.18-27.

14. Suisha F, Kawasaki N, Miyazaki S, Shirakawa M, Yamatoya K, Sasaki M, Attwood D, Xyloglucan gels as sustained release vehicles for the intraperitoneal administration of mitomycin C, International Journal of Pharmacy, 1998, 172(1-2), pp. 27–32.

15. Muller RH, Jacobs C, Kayser O, Nanosuspensions as particulate drug formulations in therapy rational for drug development and what we can expect for the future, Advanced Drug Delivery Review, 2001, 47(1), pp. 3–19.

16. Lin HH, Cheng YL, In-situ thermoreversible gelation of block and star copolymers of poly(ethylene glycol) and poly(N-isopropylacrylamide) of varying architectures, Macromolecules, 2001, pp.3710–3715.

17.Padhan A, K. Nanda ,Behera B,floating oral in-situ gel, a comprehensive approach of gastroretentive drug delivery system: a review ,IJPSR, 2019; Vol. 10(9): pp. 4034-4035.

18. D Mohanty, V. Bakshi,N. Simharaju , M. Haque and C. Sahoo: A review on in-situ gel: a novel drug delivery system. Int. J of Pharm Sci Rev and Res 2018; 50: pp. 175-81.

19. Sudhi U S, Kumar S, Nowfiya F N, Mathan S, Dharan S, Floating Oral In-Situ Gelling System: A Review. J. Pharm. Sci. & Res. Vol. 12(10), 2020, pp. 1315-1319

20. J. Patel, P. Dandagi, S.Halyalkar, and B. Desai, Formulation and Evaluation of oral floating in situ gel of cefixime trihydrate by using ß-cyclodextrin complexation technique for solubility enhancement, WJPPS, Vol 9, Issue 10, 2020, pp. 2616.

21. Linda N, Issa H, Mazen El-Hammadia and Habib A. Floating in-situ-gelling gellan formulations of metformin hydrochloride, J. Chem. Pharm. Res., 2014, 6(7), 1512-1515.

22. Bazigha K. A. Rasool, 1 A. Khalifa, Eman Abu-Gharbieh , and R. Khan, Employment of Alginate Floating In Situ Gel for Controlled Delivery of Celecoxib: Solubilization and Formulation Studies, BioMed Research International, BioMed. Res. Int., Volume 2020, pp. 3-4.

23. S. Shinde, P. Sable, B. Lodhi, S. Khan. Review Article A novel approach of gastroretentive drug delivery : in situ gel. Journal of Innovations in Pharmaceuticals and Biological Sciences, 2014; 1(1): pp. 39-59.

24. Neha V, Manoj B. Gastro Retentive In situ Gel Formulation – An Overview. International Bulletin of Drug Research, 2013; 3(5): 69–82.

25. Patel D., Patel D, and Patel C., Formulation and Evaluation of Floating Oral In Situ Gelling System of Amoxicillin, ISRN Pharmaceutics,Vol .2011, pp. 3-7.

26. Jivani R., Patel C., Patel D., and Jivani N., Development of a Novel Floating In-situ Gelling System for Stomach Specific Drug Delivery of the Narrow Absorption Window Drug Baclofen, IJPR (2010), 9 (4), pp. 360.

27. P. Mukesh, P. Alpesh , Nidhi R , and Govind V, Design and Development of Novel Floating In Situ Gel of Amoxicillin for the Treatment of Peptic Ulcer Disease Caused by Helicobacter pylori, Acta Scientific Pharmaceutical Sciences 5.9 (2021), pp. 3-4.