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A REVIEW ON FLOATING ORAL IN-SITU GELLING SYSTEM

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ABSTRACT

Due to the incomplete release of the active ingredient and the short residence time at the absorption site, drugs with a narrow absorption window in the gastrointestinal tract (GIT) are usually available to the extremities when administered orally. They are designed for high density and can swell because they allow the drug to stay in the stomach for a longer time. Oral fluids are more prone to low bioavailability because they are expelled from the stomach when they pass through the stomach/duodenum faster. Gastrointestinal retention that releases liquid immediately can be eliminated by formulating them as oral gels in situ, as they are the best way to overcome the problem of overdose. This mechanism becomes a gel floating in the stomach contents. In this way, greater maintenance and lasting relief are achieved. This is useful for the systemic and local effects of injected drugs. This review provides a brief overview of the preliminary in-situ oral floating gel studies conducted by different scientists on a series of drugs and polymers.

Keywords: Floating Drug Delivery, Gastric Retention Time, In-Situ Gel.

I. INTRODUCTION

The floating drug delivery system is one of the latest drug delivery systems. Various dosage forms are manufactured as floating gastrointestinal retention systems, such as microspheres, microspheres, tablets, capsules, films, etc. The in-situ gel system is used in various routes of administration, such as oral, nasal, ocular, oral, rectal, vaginal, and Polymer drug delivery systems formed in situ have many advantages, such as: ease of administration, higher local bioavailability, reduced dosing frequency, better patient compliance, and simpler manufacturing process, so they are advantageous. Graph. Thus, the buoyancy in the stomach can be maintained for a long time without affecting the emptying speed of the stomach. When the gel thus formed floats in the gastric juice, the drug is slowly released from the floating gel at a desired rate. After the drug leaves the flotation system, the remaining part is emptied from the stomach. It can increase TRB and control fluctuations in plasma drug concentration (PCD). The floating system is a controlled or sustained release dosage form with similar characteristics. Hydrophilic matrix and hydrodynamic balance system (HBS) because they form a low-density polymer gel barrier on the outer surface. The drug is slowly released in the form of a matrix, as is the case with a conventional matrix. This form can remain afloat (gastric contents 8-1) without affecting the various polymer systems used to deliver drugs in dosage forms. Among these polysaccharides, polymethacrylate and hydrocolloid cellulose ether polymers are the most popular, especially in 1968. The in-situ floating gelling carrier composition prolongs the effect of the drug, improves the patient's condition and reduces the frequency of administration, t, compared with the conventional drug delivery system. Efficient extension technology Residence time to increase the bioavailability of the drug. Floating drug delivery system means retention, due to its low density floating on the surface of the stomach and producing a sustained controlled release effect. Residue collection window It can also be used for drugs that have an alkaline pH in the intestine and will not be absorbed due to insolubility. FDDS can be used for drugs required for local gastric exposure. The density of the feed system is at the bottom. The higher density delivery system first settles in the stomach, then absorbs water, swells, and then floats. By reducing the density of the system. However, with such a system, it is possible to empty the stomach contents of the system before the start of flotation. The mechanism that causes air to accumulate in the system may have its limitations.

CLASSIFICATION OF FLOATING DRUG DELIVERY SYSTEMS

1. **Effervescent systems**:

These floating delivery systems use matrices made of swellable polymers, such as methylcellulose or polysaccharides, such as chitosan and effervescent ingredients, sodium bicarbonate and citric acid or tartaric acid, or have liquids that vaporize at body temperature The matrix of the chamber. Gas can be injected into the swimming room. Obtained by evaporating organic solvents (such as ether or cyclopentane) or carbon dioxide. The result of a violent reaction between organic acids and carbonate-bicarbonate. The matrix is made in such a

way that when it reaches the stomach, due to the acidity of the stomach contents, carbon dioxide is released and encapsulated in a gel-like hydrocolloid. It is developed to produce carbon dioxide.

2. **Non-effervescent systems**:

Foamless floating drug delivery systems are usually made of highly swelled or gelled polysaccharides or matrix forming polymers, such as polyacrylates, polycarbonates, polystyrenes, and polymethacrylates. In the stomach environment, the relative shape integrity and packing density are less than one. The air entrained in the swelling polymer makes these dosage forms buoyant. The most commonly used fillers in these systems include hydroxypropyl methylcellulose polyacrylate (HPMC), polycerate, carbomer, sodium alginate, calcium chloride, polyethylene oxide, and polycarbonate.

Factors affecting the floating drug delivery system

- ✓ **Density:** The gastric retention time (GRT) is a density-dependent function of the dosage form.
- ✓ **Size & Shape:** Dosage units with a diameter of more than 7.5 mm are said to have an increased GRT that can compete with units with a diameter of 9.9 mm. Compared with other forms, (KSI) has a better GIT retention rate of 90-100% after 24 hours.
- ✓ **Fed or Unfed State:** Fasting, gastrointestinal motility is characterized by a strong motor activity phase or migratory myoelectric complex (MMC) every 1.5-2 hours. MMC removes undigested material from the stomach. If the administration time of the preparation is consistent with the administration time of MMC, the TRB of the device is expected to be very short; however, in the energy state, MMC lags behind and TRB lags longer.
- ✓ **Nature of the meal**: Feeding indigestible fatty acid salt polymers can change the gastric motility structure and make it enter the postprandial state, thereby reducing the rate of gastric emptying and prolonging drug release.
- ✓ **Caloric Content:** A high-protein and high-fat diet can increase TRB from 4 hours to 10 hours.
- ✓ **Frequency of feed:** Due to the low frequency of MMC, the TRB of continuous meals increases by more than 400 minutes compared with single meals.
- ✓ **Gender**: Regardless of weight, height, and height, the average dynamic BRT with meals (3.4 ± 0.4 hours) is lower than that of women of the same age and race (4.6 ± 1.2 hours).
- ✓ **Age:** For the elderly, especially those over 70, GRT takes much longer.
- ✓ **Posture:** The ORR may be different for outpatients in the upright and supine positions.
- ✓ **Concomitant drug administration:** Anticholinergic drugs such as atropine and atropine opioids such as codeine and prokinetic drugs such as metoclopramide and cisapride.

NEED OF FLOATING DRUG DELIVERY SYSTEM:

Oral dosage forms can cause problems with low bioavailability because they are quickly excreted from the stomach, especially for drugs that are less soluble at the alkaline pH of the intestine. Similarly, when the drug is quickly emptied and there is not enough living space, the drug will act locally in the stomach. Time is in the stomach. Therefore, increase the frequency of dosing in this case. To avoid this problem, a floating drug delivery system was developed. In situ oral gel system, also known as system. Provides a convenient method for the controlled delivery of drugs to the stomach and increases gastric retention. Compared to liquids, the floating dosage forms of tablets/capsules are stable, but the problem is that they must be swallowed whole. If the dose is adjusted, it must not be violated. Half, because they are also designed for controlled release and buoyancy. The capacity also depends on the size of the tablet. Elderly patients, children, some adults and patients with certain diseases have difficulty swallowing, so it is difficult to swallow the tablet/capsule dosage form. Even in the case of dosage adjustments, these floating solid dosage forms should have different concentrations. When the gelling solution of a specific environment forms a gel on the surface of the gastric juice (because its density is lower than the gastric contents). This method uses a low-viscosity solution that changes the polymer conformation when in contact with gastric juice and forms a viscous gel with a lower density than gastric juice. They just provide the required retention in the stomach to prolong the contact time. But it can also lead to slow and sustained release of the drug.

IN SITU GELLING SYSTEM: Compared with the problems commonly encountered in semi-solid dosage forms, this new drug delivery system greatly promotes the ease of administration, the delivery of precise doses, and

the increase in the residence time of the drug in contact with the mucosa. Various incentives, such as pH changes, temperature regulation, and solvent exchange.

Smart polymer systems are promising drug delivery vehicles; these polymers undergo a sol-gel transition after injection. Since the early 1970s, natural and synthetic polymers have been studied for controlled release formulations. The advantages of using biodegradable polymers in clinical applications are obvious. Various natural polymers and synthetic materials are used to prepare the preparations. Develop the formulation of the previous in-situ drug delivery system.

Mechanism of floating oral in situ gel: Various attempts have been made to increase the residence time of dosage forms in the stomach, including floating dosage forms (gas generating systems and swelling or swelling systems), mucoadhesive systems, high-density systems, high-density systems, and modified gastric systems. A device that delays gastric emptying and a drug that slows down gastric emptying are given at the same time. Among them, the floating metering system is the most widely used. Long-term effects on gastric emptying. When the system is hovering over the contents of the stomach, the drug is slowly released from the system at the required rate. After the drug is released from the system, the remaining system is emptied from the stomach, leading to an increase in TRB and better control of fluctuations in the plasma concentration of the drug. However, in order for the dosage form to safely float above the surface of the food tube, a minimum of buoyancy (F) is required in addition to the smallest stomach contents (which is necessary to fully realize the principle of maintaining buoyancy). The kinetics of a new device for determining the weight obtained has been reported in the literature. The working principle of the device is to continuously measure the force, which is equal to F (as a function of time), the force required to keep an object in the water. The object swims better when F. The device helps to optimize the FDDS in terms of the stability and durability of the buoyancy generated to avoid the inconvenience caused by unpredictable changes in the buoyancy in the stomach.

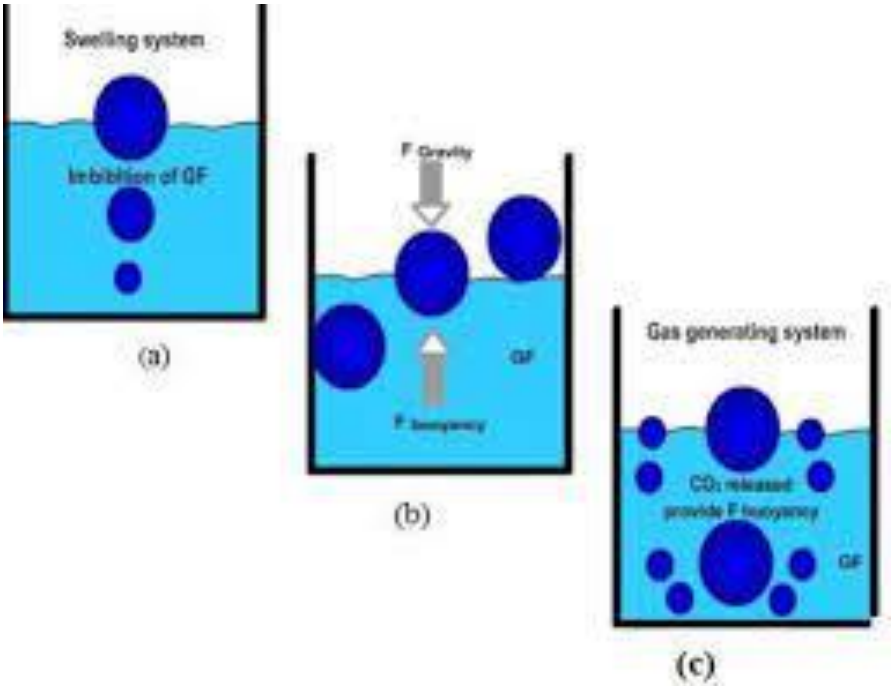

Fig 1- Mechanism of floating systems

In situ formation based on physiological stimuli:

- **Thermally triggered system -** Pluronic's are poly (ethylene oxide)-poly (propylene oxide)-poly (ethylene oxide) (PEO-PPOPEO)-triblock copolymers. They are liquid at low temperatures, but they form heat when heated. Carrier. It's a mess. These polymers are suitable for the transformation of in situ gelled micelle packing. Positive temperature-sensitive hydrogels have a higher critical solution temperature (UCST), which shrinks below UCST when cooled. Copolymers of poly (acrylic acid) (PAA) and polyacrylamide (PAAm)) or copolymers of acrylamide and butyl methacrylate show a positive temperature dependence of expansion. The most common is a thermo-reversible gel made of poly (ethylene oxide)-b-poly (propylene oxide)-b-poly(ethylene). Oxide) (Pluronix, Tetronix, Poloxamer). The polymer solution is a free-flowing liquid at

room temperature and a gel at body temperature. Like Pro-Lastine, it undergoes an irreversible sol-gel transition. When administered as a solution, the material will form a solid, stable gel within minutes. It stays at the injection site and the absorption time varies from less than a week to several months. The system can be easily inserted into the required body cavity.

- **pH triggered systems -** Another type of in-situ gelation based on physiological stimuli is gelation caused by pH changes. All pH-sensitive polymers contain acid or base side groups that can accept or release protons in response to changes in environmental pH. A variety of ionizable groups are called polyelectrolytes. As the external pH value increases, the swelling of the hydrogel increases with the increase of weakly acidic (anionic) groups, but it decreases when the polymer contains weakly basic (cationic) groups. They are based on PAA (Carbopol®, Carbomer) or its derivatives. In addition, a low-viscosity solution of polyvinyl acetal diethylamino acetate (AEA) forms a pH 4 hydrogel under neutral pH conditions. Drugs made in liquid solutions have several limitations, including limited bioavailability and a tendency to be easily eliminated. To minimize these factors and maximize the delivery of this drug, prepare a polyacrylic acid (PAA) solution with a pH of 7.4 that gels the eyes before being neutralized by tear fluid. This problem is solved by a partial combination of PAA and HPMC (a viscosity-improving polymer), which causes the mixture of pH-sensitive polymers to dissolve at pH 4 and gel at pH 7.A mixture of poly (methacrylic acid) (PMA) and polyethylene glycol (PEG) is also used as a pH sensitive system to achieve gelation.

In situ formation based on physical mechanism:

- **Swelling -** Formation in situ may also occur when the material absorbs moisture from the environment and expands to occupy the required space. One such substance is Myverol 18-99 (glycerol monooleate), a polar lipid 1400 that swells in water to form a lyotropic liquid crystal phase. It has some bio adhesive properties and can be broken down by enzymes in the body.
- **Diffusion -** This process involves the diffusion of solvent from the polymer solution to surrounding tissues and causes the deposition or solidification of the polymer matrix. N-Methylpyrrolidone (NMP) has proven to be a suitable solvent for this type of system.

In situ formation based on chemical reactions:

The chemical reaction leading to in-situ gelation can include precipitation of inorganic solids from supersaturated ionic solutions, enzymatic processes, and photoinitiated processes.

- **Ionic cross linking –** Polymers can undergo phase changes in the presence of various ions. Some polysaccharides belong to the ion-sensitive category. Although k-carrageenan forms a hard and brittle gel with a small amount of K +, i-carrageenan mainly forms an elastic gel in the presence of Ca2 +. Gellan gum, under the trade name Gelrite, is an anionic polysaccharide that gels in situ in the presence of monovalent and divalent cations (including Ca2+, Mg2+, K+, and Na). Gels with low methoxy pectin content may be caused by divalent cations, especially Ca2+. Due to the interaction with the glucuronic acid block in the alginate chain, alginic acid will also gel in the presence of multivalent cations such as Ca2+. Some advantages over chemical and photochemical methods. For example, enzymatic processes work efficiently under physiological conditions and do not require potentially harmful chemicals such as monomers and initiators. Intelligent stimulus-sensitive delivery systems have been studied using hydrogels that can release insulin. The cationic pH-sensitive polymer containing immobilized insulin and glucose oxidase can swell in response to blood glucose levels and release the captured insulin in a pulsating manner. The adjustment of the amount of enzyme also provides a convenient mechanism to control the rate of gel formation, thereby allowing the mixture to be injected before the gel is formed.
- **Enzymatic cross-linking –** In situ formation catalysed by natural enzymes has not been extensively studied, but seems to have some advantages over chemical and photochemical methods. For example, enzymatic processes work efficiently under physiological conditions and do not require potentially harmful chemicals such as monomers and initiators. Sensitive delivery systems have been studied using hydrogels that can release insulin. Cationic pH-sensitive polymers containing immobilized insulin and glucose oxidase can swell in response to blood glucose levels and release trapped insulin in a pulsating manner. A mechanism to control the speed of the gel, allowing the introduction of the mixture before the gel is formed.
- **Photo Polymerisation** - Photopolymerization is widely used to form biological materials in situ. Reactive and initiator monomers or macromer solutions can be introduced into the tissue site, and electromagnetic

radiation can be used to form a gel. Acrylates or similar polymerizable functional groups are generally used as polymerizable groups in single monomers and macromers because they undergo rapid photopolymerization in the presence of a suitable photoinitiator. Generally, long-wave ultraviolet and visible light wavelengths are used. Ketones such as 2,2-dimethoxy-2-phenylacetophenone are widely used as UV polymerization initiators, while camphor quinone and ethyl eosin initiators are commonly used in visible light systems. Degraded by chemicals or photopolymerization systems, when injected into the desired site by injection, the gel uses fiber optic cables to photopolymerize in situ, and then release the drug for an extended period of time. This reaction provides a high polymerization rate at physiological temperature. In addition, the system can be easily placed in a complex volume to form an implant.

Table 1: Commercial Formulations of In Situ Polymeric Systems

Dosage Form	Drugs	Brand Name	Company; Country
Ophthalmic	Timolol maleate	Timoptic-XE	Merk & Co
Regel: depot-technology	Paclitaxel	Oncogel	Macromed's drug del
Injectable depot formulation	Interleukin -2	Cytoryn	Macromed's drug del
Ophthalmic	Lidocaine HCl	Akten	Nil
Ophthalmic solution	Azithromycin	Azasite	Insite Vision

Table 2: Marketed Products of FDDS

Dosage Form	Drugs	Brand Name	Company; Country
Floatingk Controlled Release Capsule	Levodopa, Benserazide	MODAPAR	Roche Products, USA
Floating Capsule	Diazepam	VALRELEASE	Hoffmann-LaRoche, USA
Effervescent Floating Liquid alginate Preparation	Aluminium hydroxide, Magnesium Carbonate	LIQUID GAVISON	Glaxo Smith Kline, INDIA
Floating Liquid alginate Preparation	Aluminium-Magnesium antacid	TOPALKAN	Pierre Fabre Drug, France
Colloidal gel forming FDDS	Ferrous Sulphate	Conviron	Ranbaxy, IINDIA
G;2as-generating floating Tablets	Ciprofloxacin	CIFRAN OD	Ranbaxy, INDIA
Bilayer floating Capsule	Misoprostil	CYTOTEC	Pharmacia, USA

RECENT ADVANCES: One of the challenges facing the pharmaceutical industry today is to find effective treatments that are acceptable to doctors and patients. If delivery systems are to provide viable alternatives to drugs currently administered through other routes, they must also contribute to better treatment outcomes. In situ gel formulations are one of the most complex drug delivery systems. Some biodegradable polymers are used to make gels in situ, but there are manufacturing problems, processing difficulties, and the use of organic solvents to make them (especially for systems based on synthetic polymers), explosive effects and unreproducible drug release kinetics. Natural polymers conform to the characteristics of ideal polymers, but the reproducibility between batches is difficult, so synthetic polymers are used. Biodegradable block copolymers based on poly(ester-ester) sugar h are available as polyethylene oxide-poly (lactic acid) i. Copolymer (PEO-PLA), poly (ethylene oxide)-poly(caprolactone) I. (PEO-PCL), poly (ethylene glycol)-poly(lactide-co-glycolide)-poly (ethylene glycol) I. Copolymers (PEG-PLGA-PEG) can also be used to form in-

situ injection hydrogels with better biocompatibility, biodegradability, lower explosiveness, better mechanical resistance and processability. A therapeutic agent that requires a complex formulation to be effectively administered. The ethyl ester of N-stearoyl-L-alanine (m), when mixed with vegetable oils and biocompatible hydrophilic solvents, will form an injectable, forming an organogel in situ. After subcutaneous injection, the organogel containing leuprolide gradually decomposes and releases leuprolide within 14-25 days.

Future aspects: The management of Chinese medicinal materials is a new field of pharmacy. The use of floating medicinal herb delivery systems is a new method for better delivery. For this reason, there is a good opportunity to study the GI transportation profile. Adding new products with significant patient benefits with the advent of FDDS, products that can release drugs within 24 hours have been developed. Some herbs that can be administered as a floating drug delivery system include:

- **Black Myrobalan** –

The water extract of black myrobalan (called Terminalia chebula Retz) has consistent antibacterial effects against 10 clinical Helicobacter pylori species.

- **Ginger –**

Ginger root (familiar with turmeric) is traditionally used to treat gastrointestinal diseases, such as motion sickness, indigestion, and hyperemesis gravidarum. It also has a chemo preventive effect in animal models.

- **Turmeric –**

Curcumin is a polyphenol chemical extracted from turmeric (known from Curcuma longa L.), which can prevent gastric and colon cancer in rodents. Several chemo preventive mechanisms have been proposed, but the effect of curcumin on the growth of Helicobacter pylori has not been reported.

- **Licorice –**

In a recent study by the German Institute of Medical Microbiology and Virology, researchers found that licorice extract is effective against Helicobacter pylori strains resistant to clarithromycin, which is commonly used in all three antibiotic therapies One of the antibiotics.

II. CONCLUSION

In summary, the main requirements for a successful controlled release product focus on the increased patient compliance provided by the in-situ gel. The use of in-situ polymer gels to control the release of various drugs offers many advantages over traditional dosage forms. Active ingredient release, good stability and biocompatibility characteristics make the gel formulation very reliable in situ. The use of water-soluble and biodegradable polymers for in-situ gel formulations can make these more acceptable and better drug delivery systems. The development potential of oral liquids for sustained-release drugs is huge. This floating gel method is suitable for drugs with a narrow absorption window in the stomach or drugs that act locally on the stomach. Their fixed-dose forms (tablets or capsules) can be used as floating gels.

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