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FLOATING *IN-SITU* GELS: AN INNOVATIVE ORAL DRUG DELIVERY APPROACH

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ABSTRACT

Floating oral *in-situ* gels are an advanced gastro-retentive drug delivery system designed to prolong gastric residence time and achieve controlled drug release. These formulations exist as low-viscosity solutions that transform into buoyant gels upon contact with gastric fluids, triggered by physiological stimuli such as pH change, temperature modulation or ionic cross-linking. Polymers like sodium alginate, gellan gum and (HPMC) are commonly used to ensure optimal gel strength, stability and sustained release. This system enhances the bioavailability of drugs with narrow absorption windows, maintains steady plasma concentrations and minimizes gastric irritation. Moreover, floating oral *in-situ* gels improve the therapeutic efficacy of drugs with short half-lives and reduce fluctuations in drug concentration. Owing to their ease of administration, cost-effectiveness, scalability and improved patient compliance, floating oral *in-situ* gels offer a promising and efficient platform for site-specific and controlled gastric drug delivery.

KEYWORDS: Floating system, *In-situ* gel, Polymers.

INTRODUCTION

FDDS was first described by Davis in 1968. The floating drug delivery system is one of the modern ways of delivering medications. Numerous dosage forms, such as microspheres, microbeads, tablets, capsules, films etc., have been developed in the form of gastro-retentive floating systems. The latest innovation in floating DDS is the *in-situ* gelling system. There are

several ways to administer the *in-situ* gelling system, including parenteral, nasal, ocular, peroral, rectal, vaginal and oral routes. Numerous benefits come with *in situ* forming polymeric drug delivery systems, including lower dosage frequency, more local bioavailability, easier administration, better patient compliance and a simpler, more affordable production process. Gastro retentive FDDS stay buoyant in the stomach for a long time without influencing the gastric emptying rate because their bulk density is lower than that of gastric fluid. The medicine is gradually released from the gel at the appropriate frequency once the gel has formed and it floats on stomach fluid. Following the drug release from the floating system, the stomach remaining contents are evacuated. This may increase GRT and regulate fluctuations in plasma drug concentration (PCD). This type of delivery system is of great value for drugs which get absorbed from upper part of the stomach. The FDDS are especially helpful for medications that need to have a local action in the stomach.[1,2]

Need of Floating drug delivery system

Oral dosage forms pose low bioavailability problems due to their rapid gastric transition from the stomach, especially in case of drugs which are less soluble at an alkaline pH of the intestine. Likewise, medications that generate their local effect in the stomach are quickly evacuated and do not have enough time to remain in the stomach. Therefore, the frequency of dosage administration is raised in these situations. To overcome this issue, a floating drug delivery system has been developed.[3,4]

ADVANTAGES

- Increased bioavailability and curative efficiency of drugs and economic use of dosage.
- The prolonged stomach residence time of floating dosage forms, such as tablets or capsules, improves drug absorption by enabling them to stay in solution at the absorption site for a longer period of time, even in the alkaline pH of the intestine.
- Improved patient compliance by decreasing dosing frequency and ease of administration.
- FDDS are advantageous for drugs which are absorbed through the stomach e.g. ferrous salts, antacids.
- Controlled delivery of drugs. It minimizes the gastric or mucosal irritation by releasing drug slowly at controlled rate.
- Acidic substance like aspirin produce irritation on the stomach wall when come in contact with it thus FDDS formulation may be helpful for the administration of aspirin and other similar drugs.

- FDDS can be used in the treatment of gastrointestinal disorders such as gastroesophageal reflux.
- Provide Site-specific drug delivery system.
- Floating dosage forms are advantageous in case of vigorous intestinal movement and in diarrhoea by keeping the drug in floating condition in stomach to get a relatively better response.
- Simple and conventional equipment required for manufacture.
- Slow release of the drug from FDDS dosage form into the body minimizes the counter activity leading to higher drug efficiency.
- FDDS enhances the pharmacological effects and improves the clinical outcomes by reducing the drug concentration fluctuations over a critical concentration.
- Through FDDS better therapeutic effect of short half-life drugs can be achieved.[5,6]

LIMITATIONS

- The major disadvantage of floating system is requiring a high level of fluids in the stomach for drug delivery to float and work efficiently.
- These systems are not feasible for those drugs that have solubility or stability problem in GI tract.
- Drugs such as Nifedipine, Propranolol etc. which are well absorbed throughout GIT and which undergoes first pass metabolism are not be desirable candidate.
- Drugs (like NSAIDS) that can cause irritation and lesions to gastric mucosa are not suitable to be formulated as floating drug delivery systems.
- The drug candidates that are unstable in the stomach acidic environment are not suitable to be incorporated in the FDDS systems.
- Ability to float relies in the hydration state of dosage form.
- The mucus present on the walls of the stomach is in a state of constant renewal which results in unpredictable adherence.
- Dosage form requires faster swelling properties as well as complete swelling of the system must be achieved before the gastric emptying time.[5,7]

Drug Candidates Suitable for FDDS

- Drugs with narrow absorption window in Gastrointestinal tract. Ex: Methotrexate, Levodopa, Repaglinide, Riboflavin and Furosemide.
- Drugs acting locally in the stomach. Ex: Antacids, Anti-ulcer drugs, Misroprostol.

- Drugs having low solubility at high pH values. Ex: Diazepam, Chlordiazepoxide, Verapamil.
- Drugs having unstable properties in the intestinal or colonic environment. Ex: Captopril, Ranitidine HCl, Metronidazole, Metformin HCl.
- Drugs caused imbalance of normal colonic microbes. Ex: Antibiotics against H. Pylori, Amoxicillin Trihydrate.

Drug Candidates Unsuitable for FDDS

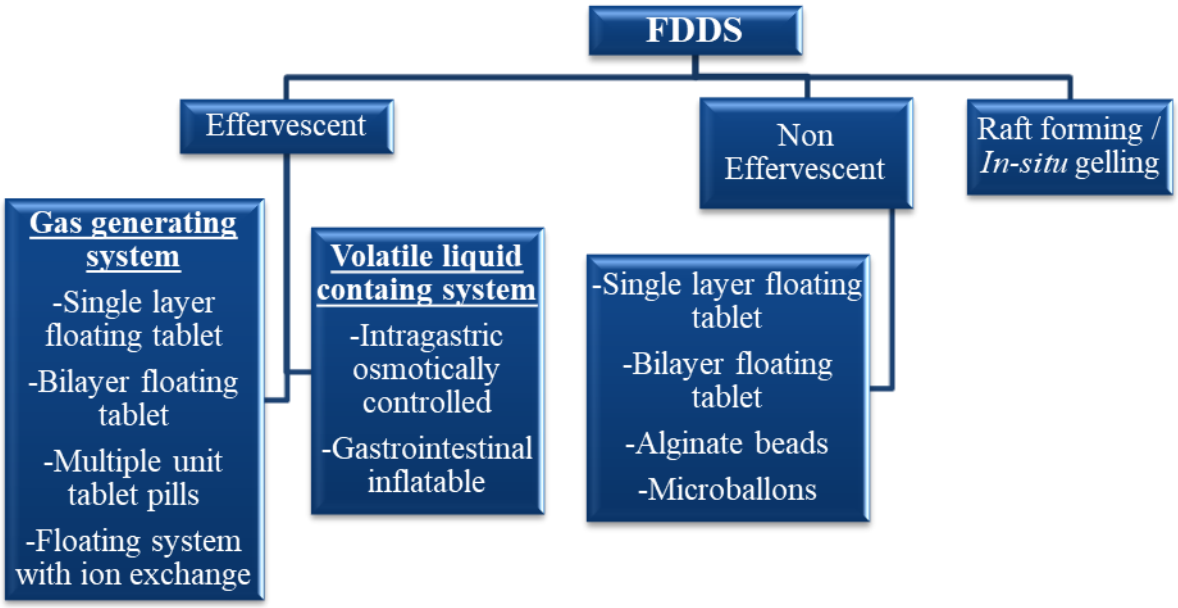
- Drugs having very limited acid solubility. Ex: Phenytoin
- Drugs that suffer instability in the gastric environment. Ex: Erythromycin
- Drugs that are used for selective release in the colon. Ex: 5- amino salicylic acid and corticosteroids.[8]

Factors affecting FDDS

- **Density:** The density of the dosage form should be less than the gastric contents (1.004 g/mL).
- **Size and Shape:** Dosage forms with diameters exceeding 7.5 mm show increased GRT compared to those with a diameter of 9.9 mm. Tetrahedron and ring-shaped dosage forms with flexural moduli of 48 and 22.5 kilopond per square inch (KSI) respectively, exhibit superior GI transit with 90 to 100% retention over 24 hours compared to other shapes.
- **Single or Multiple unit formulation:** Multiple unit formulations provide a more predictable release profile and exhibit minimal performance impairment due to unit failures, enabling the co-administration of units with varying release profiles as opposed to single unit dosage forms.
- **Fed and Unfed state:** Under fasting conditions, gastrointestinal motility exhibits strong motor activity every 1.5 to 2 hours, leading to a short GRT if formulation administration coincides with the migrating motor complex (MMC). Conversely, in the fed state, the MMC is delayed, resulting in a significantly longer GRT.
- **Nature of Meal:** Fatty acid salts or indigestible polymers can alter the stomach's motility pattern to a fed state, which lowers the rate of gastric emptying.
- **Caloric content:** GRT can be enhanced by 4–10 hours by consuming a rich protein and fat meal.
- **Frequency of feed:** Due to the low frequency of MMC, the GRT can increase by more than 400 minutes when many meals are provided as opposed to a single meal.

- **Gender:** Males' mean ambulatory GRT (3.4 ± 0.6 hrs) is lower than that of their female counterparts of the same age and race (4.6 ± 1.2 hrs), irrespective of body surface, height, or weight.
- **Age:** The GRT is extended in the elderly, particularly in those over 70.
- **Posture:** GRT may alter depending on the patient's reclined or standing mobility status.
- **Concomitant drug administration:** Prokinetic agents like metoclopramide and cisapride, anticholinergic agents like atropine and propantheline opiates like codeine.
- **Disease state:** The GRT increases by diabetes, hypothyroidism, and stomach ulcers. Duodenal ulcers and hyperthyroidism reduce GRT.[9,10]

CLASSIFICATION OF FDDS



List of Marketed Floating Dosage Forms

Table 1: List of the various marketed preparations of Floating Drug Delivery system.

Sl. No.	Product	API	Dosage Form
1	MODAPAR	Levodopa, Benserazide	Floating controlled release capsule
2	PROLOPA	Levodopa, Benserazide	Floating controlled release capsule
3	VALRELEASE	Diazepam	Floating capsule
4	TOPALKAN	Aluminium-Magnesium antacid	Floating liquid alginate preparation
5	LIQUID GAVISON	Aluminium hydroxide, Magnesium carbonate	Effervescent floating liquid alginate preparation
6	ALMAGATE FLATCOAT	Aluminium-Magnesium antacid	Floating dosage form

7	CYTOTEC	Misoprostol	Floating tablet
8	CONVIRON	Ferrous sulfate	Colloidal gel forming FDDS
9	CIFRAN OD	Ciprofloxacin	Effervescent floating tablet
10	ZANOCIN OD	Ofloxacin	Effervescent floating tablet
11	OFLIN OD	Ofloxacin	Gas generating floating

IN-SITU GELLING SYSTEM

This unique drug delivery system significantly improves ease and convenience of administration. This unique drug delivery system significantly improves administration ease and convenience, delivers precise doses and extends the drug's residence duration in contact with the mucosa, all of which are concerns frequently encountered with semi-solid dosage forms. *In-situ* gel formation occurs due to one or combination of different stimuli like pH change, temperature modulation and solvent exchange. Smart polymeric systems represent promising means of delivering the drugs; these polymers undergo sol-gel transition, once administered. From the early 1970's natural and synthetic polymers began to be investigated for controlled release formulations. The advantages of using biodegradable polymers in clinical applications are apparent. Various natural and synthetic polymers are used for formulation development of in situ forming drug delivery systems.[11,12]

Advantages of *In-Situ* Gelling System

- Ease of administration.
- Sustained drug delivery.
- Increase local bioavailability.
- Reduced dosing frequency.
- Reduce the fluctuation of drug concentration.
- Improved patient compliance and comfort.
- Its production is less complex and so lowers the investment.

Floating oral *in-situ* gel is a low-viscosity polymer solution, when it comes into contact with stomach fluids, alters polymeric structure and forms a strong viscous gel with a density lower than the gastric fluids. Ionic cross-linking, changes in pH and temperature changes can all cause the gelation.[13]

Mechanism of *in-situ* gelling system

These are liquid aqueous solutions before the administration, but they gel when physiological conditions are met. Temperature modulation, pH change and ionic cross linking are a few

potential processes that result in *in-situ* gel formation. Gellan, pectin, sodium alginate and other polymer solutions contain divalent ions complexed with sodium citrate, which are broken down in the stomach's acidic environment to liberate free divalent ions (Ca^{+2}), which results in the *in-situ* gelation of an oral solution. Double helical segments aggregate to create a dimensional network by complexation with cations and hydrogen bonding with water, resulting in the development of double helical junction zones.[14]

Mechanism of Floating *in-situ* gelling system

During gastric retention, the floating drug delivery system (FDDS) maintains floating while releasing the drug at a controlled rate. Following complete drug release, the residual system is expelled from the stomach along with minimal gastric contents. A minimum floating force (**F**) is essential to ensure consistent buoyancy of the dosage form on the gastric fluid surface.

A novel apparatus for measuring the **resultant weight** of floating systems has been reported, which continuously records the force equivalent to **F** as a function of time. Higher positive values of **F** denote superior buoyancy (Fig. 2). Evaluation of floating force kinetics is critical for optimizing FDDS formulations with respect to the stability and persistence of floating behavior, thereby reducing the impact of intragastric variations.[15]

$$F = F_{buoyancy} - F_{gravity}$$

$$= (Df - Ds)\, gv$$

Where, F = total vertical force Df = fluid density

Ds = object density v = volume

g= acceleration due to gravity

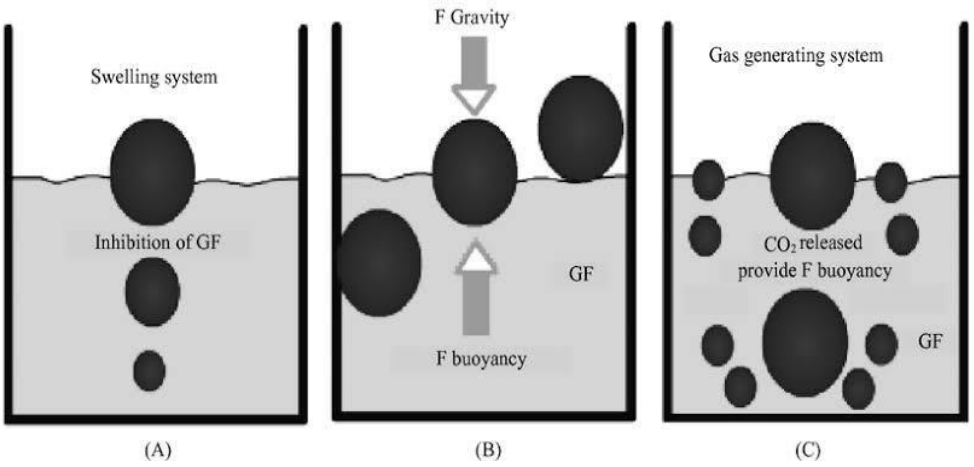


Figure 1: Mechanism of Floating *in-situ* gel.

Approaches to produce Floating *In-situ* gel system

- Based on physical changes
  - Swelling
  - Diffusion

- Based on chemical changes
  - Ion cross linking
  - Enzymatic cross linking
  - Photo polymerization

- Based on physiological stimuli
  - Temperature
  - pH

Based on physical changes[16]

- **Swelling**

In-situ gel formation involves polymeric lipids absorbing water and expanding to create a desired space. An example is myverol 18-99 (glycerol mono-oleate), a polar lipid that swells in water to form liquid crystalline structures. It exhibits bioadhesive properties and can be degraded *in-vivo* by stomach enzymes.

- **Diffusion**

In this method the diffusion of solvent from polymer solution into surrounding tissue and results in precipitation or solidification of the polymer matrix. The solvent of N-methyl pyrrolidone (NMP) is useful for such a system.

Based on chemical changes[17]

- **Ion cross linking**

Ion-sensitive polysaccharides like sodium alginate, iota carrageenan, gellan gum, and pectin form *in-situ* gels in the presence of ions such as K^+, $Ca^{2+,}$ Mg^{2+} and Na^+. These gels are created by administering a solution that contains a gelling agent, leading to gel formation in the stomach under specific conditions. The process involves polymer solutions, like sodium alginate, that trigger gelation through ionic complexation with divalent ions (Ca^{2+}) released from Na-citrate in the acidic stomach environment. This results in cross-links between polymer chains, forming a matrix structure. The *in-situ* gel comprises a double helical network stabilized

by cation complexation and hydrogen bonding with water, allowing for slow and controlled drug release while the residual gel is later emptied from the stomach.

- **Enzyme 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.

- **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.

Based on physiological stimuli[18]

- **Temperature**

Hydrogels described are liquid at room temperature (20-25ºC) and gel upon contact with body fluids (35-37ºC), due to temperature increases. This property takes advantage of the temperature-induced phase transition, where polymers exhibit significant changes in solubility related to lower critical solution temperature (LCST). Negative temperature-sensitive hydrogels experience unfavorable hydrogen bonding with water, leading to dehydration and a hydrophobic structure. Conversely, some amphiphilic polymers show increased LCST and form gels via polymer-polymer interactions as temperature rises, illustrated by the behavior of cross-linked N-isopropylacrylamide-co-butylmethacrylate (P(NIPAAmco-BMA)).

- **pH**

pH-sensitive polymers are those that react to variations in pH and have acidic or alkaline functional groups. Materials that respond to pH can be used to address the pH, which is a significant signal. A change in the pH causes the fluid to gel. A polyelectrolyte is a class of polymers that include a lot of ionizable groups. When weakly acidic (anionic) groups are present in the polymer, hydrogel swelling rises as the external pH rises; nevertheless, when weakly basic (cationic) groups are present, hydrogel swelling falls. As an anionic polymer,

consider carbomer and its derivatives.

Polymers used for *in-situ* gel system[19]

The polymers selection for preparation of *in-situ* gel drug delivery system should be soluble, biologically compatible, biodegradable, having good drug-polymer linkage, good mechanical strength and inert.

Classification of Polymers of *in-situ* gel

Based on their origin, polymers are classified or the mechanism of gelation. According to a source in situ, gelling systems classified into two types:

1. Natural Polymers

Eg: Alginic acid, Carrageenan, Chitosan, Guar gum, Gellan gum, Pectin, Sodium hyaluronate, Xanthan gum, Chitosan and Xyloglucan**.**

2. Synthetic Polymers

Eg: Polyacrylic acid, PLGA, Polyvinyl pyrrolidone and Poloxamers.

3. Semi synthetic Polymers

Eg: Cellulose acetate phthalate, Ethyl cellulose, Hydroxypropyl methylcellulose and Methylcellulose.

Alginic acid or Sodium alginate[20]

A biodegradable, hydrophilic, non-toxic, linear block copolymer polysaccharide consists of β-D-mannuronic acid and α-L-glucuronic acid residues joined by 1,4-glycosidic linkages. It is used as a vehicle for ophthalmic formulations. Alginate transforms into a stable gel upon exposure to divalent cations (Ca^{+2}, Mg^{+2}) by cross-linking the carboxylate groups, which is not easily eroded by tear fluid.

Carrageenan[21]

It is used as a home remedy to cure a cold and cough as gelatine. Depending on the sulfate group number and position classified into three types:

- **Iota carrageenan:** It forms an elastic gel in the presence of calcium or potassium ions and completely soluble in hot water.
- **Kappa carrageenan:** It forms a 'gel' in the presence of potassium ions and shows similar properties of locust bean gum, like soluble in hot water.

- **Lambda carrageenan:** It does not induce gel formation, but it forms highly viscous solutions and is completely soluble in cold water.

Chitosan[22]

It is a biodegradable, biocompatible, thermosensitive, pH dependent, cationic, amino polysaccharide obtained by alkaline deacetylation of chitin. Gelling of chitosan occurs by pH and temperature changes. It has excellent mucoadhesive properties due to the electrostatic interaction between positively charged chitosan and negatively charged mucosal surfaces. At low critical solution temperatures due to extreme hydrophobic interactions, gels formed with electrostatic forces. At upper critical solution temperature, exhibiting polymers are used for the gelation process of chitosan. Due to availability, non-toxic, inexpensive, etc., this is the second most abundant polysaccharide using after cellulose.

Guar gum[23]

It is soluble in water but insoluble in hydrocarbons, fats, ester, alcohols, and ketones. It shows better dispersibility and forms high viscous colloidal solutions with hot and cold water with small amounts. Temperature changes cause a reversible shift in gel formation.

Gellan gum[24]

It is commercially known as Gelrite or Kelcogel, and it is a linear, water-soluble, temperature-dependent, extracellular, hetero, anionic polysaccharide; like alginate, this gellan gum form gel in the presence of metal cations (mono or divalent). Monovalent cations such as Na+or K+and divalent cations such as Ca+2 or Mg+2 induce cross-linking gelation. The gelation includes the formation of double helical junction zones followed by aggregation of the double-helical segment to form 3-D networks by complexation with cations and hydrogen bonding with water. In the preparation of in situ gels, it is one of the most commonly used polymers.

Pectin[25]

A family of cationic, linear polysaccharides comprises α-(1, 4)-D galacturonic acid residues. In the presence of H+ions, the gelation of pectin will occur, a source of mono, divalent, and trivalent ions. It is only applicable to water-soluble formulations and not for the organic solvents. Monovalent cations (alkali metal) salts of pectin and pectic acids are soluble in water. But di and trivalent cationic salts are weakly soluble or insoluble in water. When the addition of water to dry powdered pectin, clumps (i.e., semi-dry packets) formed due to its

tendency to hydrate and solubilization of cluster's done by mixing with a water-soluble carrier. The degree of methylation (DM), defined as the percentage of carbonyl groups esterified with methanol. Based on the degree of esterification, pectins classified into two categories:

- Low methoxy pectins; less than 50% of the carboxyl groups methylate the pectins.
- High methoxy pectins; more than 50% of the carboxyl groups methylate the pectins.

Sodium hyaluronate[26]

It is a water-soluble form of the sodium salt of hyaluronic acid. It is a natural, endogenous polysaccharide that supports producing collagen and maintains elasticity in the body. It also increases formulation stability and reduces the probability of oxidation.

Xyloglucan[27]

Xyloglucan is an abundant, hemicellulosic polysaccharide due to the non-toxic, biocompatible, and biodegradable nature, potentially using in several delivery systems. It is partially degraded by β galactosidase and undergoes gelation by the thermoresponsive process. When used in oral delivery shows gelation time up to minutes and allows gelation in the stomach in chilled condition. Like, poloxamer it exhibits gelation on heating/refrigerator temperature or cooling from higher heat. Xyloglucan has the gelling ability in the presence of sugars (40-65%) or alcohols over a wide pH range. Still, in the combination (20% alcohols), the sugars are substantially reduced to form a gel.

Thiomers or Thiolated chitosan[28]

Nowadays, thiol groups exhibit much higher adhesive (mucoadhesive) properties than other polymers. Thiomers interact with cysteine-rich sub-domains or mucus glycoproteins via cross linking intra-and inter-disulfide bonds by the simple oxidation process that leads to gel formation reaching the physiological environment. These are the most promising multi-functional, cationic, hydrophilic macromolecules and they also act as permeation enhancers than chitosans. It has positive charges which interact with the cell membranes causing a structural reorganization of tight junction-associated proteins. Apart from this, it also exhibits a robust, cohesive nature.

Xanthan gum[29]

Xanthan gum shows good stability at both acidic and alkali conditions and soluble in cold and hot water. It exhibits anionic nature due to the presence of both glucuronic and pyruvic acid groups.

Polyacrylic acid or PAA[30]

PAA is commercially known to be carbopol. It is widely used in ophthalmology for enhancing pre-corneal retention. It can exhibit excellent mucoadhesive properties to compare with other cellulose derivatives. Comparing different grads such as carbopol 910, 934, 940, 941, etc. concluded that 940 showed superior one.

Poly (lactic-co-glycolic acid) or PLGA[31]

It is a biocompatible and biodegradable polymer. It is a synthetic copolymer of polylactic acid (PLA) and polyglycolic acid (PGA). These systems are applied to controlled drug delivery and are available as implants, microparticles, and in situ implants in the market. PLGA is one of the most capable polymers used to fabricate drug delivery and tissue engineering applications because of its long clinical experience.

Poloxamers[32]

Poloxamines are commonly known as tetronics. These are biocompatible, tetra functional block copolymers of ethylene and propylene oxide. Four arms of PEO-PPO form X- shaped poloxamines, linked by an ethylenediamine group, and seem crucial for the osteoinductive capability of tetronics. It exploited until now for rendering temperature and pH- responsive micelles and gels dually. There is no other polymer reported to be osteoinductive itself. Hydrophilic one is more cytocompatible than hydrophobic and shows better compatibility as their molecular weight increases.

Cellulose acetate phthalate (CAP)[33]

CAP also known as pseudo latex. It is artificial latex, prepared in an aqueous medium by dispersion of a pre-existing polymer. It is pH sensitive, cross-linked polyacrylic polymers with potentially useful properties for sustained drug delivery to the eye because latex is a free-running solution at a pH of 4.4, which undergoes coagulation tear fluid, raises the pH to pH 7.4. CAP is used to monitor the ocular residence time of an ophthalmic preparation in γ-scintigraphy, and the production doesn't require the use of organic solvents.

Hydroxypropyl methylcellulose (HPMC)[34]

This is a biocompatible, thermoreversible, mucoadhesive polymer. It is a type of cellulose ether due to high swellability, thermal gelation properties, and used as hydrophilic matrices and used for oral drug delivery systems. HPMC used in combination with carbopol, enhancing the solution's viscosity while reducing the solution's acidity. HPMC goes for gelation

at higher temperatures due to the interaction between hydrophobic components of the polymer. It was playing an active role in aqueous solution formation for topical treatment of the eye.

It proved to be essential to formulate vaginal mucoadhesive film with CR of S-nitroso glutathione and effects on the gelling behavior.

Methylcellulose (MC)[35]

It is also a cellulose derivative, used as in situ gelling polymer. Several cellulose derivatives stay on liquid at low temperatures and become gel upon heating. For example, MC and HPMC's aqueous solution undergoes a phase transition into gels between 40-50 °C and 75- 90 °C, respectively. However, MC and HPMC's phase transition temperature is higher than the physiological temperature but lowered by making chemical and physical changes in the polymers. Hydrophobic interaction among molecules with methoxy groups causes gelation of HPMC and MC solutions. Polymer-polymer contact occurs between macromolecules due to hydration at a lesser temperature. The hydration is lost gradually on increasing the heat consequential in lower viscosity. At the transition where enough dehydration of the polymers takes place, they start associating, and the thickness starts rising, showing a network structure formation. At low temperature (30 °C) solution is in liquid form, and when the temperature increased (40-50 °C) and gelation occurred.

EVALUATION OF *IN-SITU* GELLING SYSTEM[36,37]

- **Determination of Drug content**

It is necessary to dissolve a specific weight of formulation equal to an amount of the medication in an appropriate medium, agitate it for the necessary period of time, filter it, and determine its drug content.

- **pH determination**

A digital pH meter can be used to measure a solution's pH and identify the ideal circumstances that promote *in-situ* gelling. Using a medium with different pH values, the impact of pH on sol gelation may be ascertained.

- ***In-vitro* gelling capacity**

Generally speaking, an *in-situ* gelling system's gelling capacity can be ascertained by creating a colored solution for visual inspection. The time it takes for *in-situ* gel formation, its stiffness, and the amount of time the produced gel stays intact may all be assessed by introducing the *in-*

situ gelling formulation to a medium that mimics stomach fluid.

- ***In-vitro* buoyancy studies**

The parameters such as the time it takes for the system to float over the surface of the medium (floating lag time) and the time the formed gel continuously floats over the surface of the dissolution medium (floating time) can be estimated after adding a fixed volume of *in-situ* gelling formulation to a medium (simulating gastric fluid).

- ***In-vitro* drug release studies**

The release rate of drug from *in-situ* gel can be determined using USP dissolution rate testing apparatus II (Paddle type) or USP dissolution rate testing apparatus I (basket covered with muslin cloth) at 50 rpm. 900ml of 0.1N HCl can be used as dissolution medium and temperature of 37±0.5°C can be maintained. 5ml samples can be withdrawn at various time points for estimating the drug release using UV- Visible spectrophotometer. Same volume of fresh medium has to be replaced every time the sample is withdrawn. The drug release studies from in situ gel can also be done using plastic dialysis cell.

- **Measurement of rheological property of sol and gel**

The viscosity of the solution prepared using various concentrations of gelling agents can be determined by viscometers like Brookfield viscometer, Cone & plate viscometer, etc. The viscosity of the formed gel can also be determined to estimate the gel strength.

- **Water uptake study**

After the solution turns into gel, it is separated from the medium and any extra medium is wiped using tissue paper. It is necessary to record the gel's starting weight. Once more, the gel must be exposed to the medium/distilled water. This procedure must be repeated every 30 minutes in order to record the weights of the gel at each interval after the excess medium/distilled water has been removed using filter paper. It is necessary to periodically record the weight gain brought on by water absorption. For *in-situ* gelling type floating formulations, the effects of pH, gelling agent/cross-linking agent concentration on viscosity, *in-situ* gelation character, floating ability and drug release may be investigated.

- **Gel strength**

This parameter is assessed using a rheometer and a beaker filled with a predetermined volume of gel solution. The rheometer probe is pushed through the gel by raising this beaker. It is

possible to calculate the change in the load on the probe as a function of the probe's merging depth below the gel surface.

Table 2: Research activities on oral floating *in-situ* gel.

Author	Drugs	Category	Reference No.
Jayswal et al.	Cimetidine	Antihistaminic	[38]
Jivani et al.	Baclofen	Skeletal muscle relaxant	[39]
Itoh et al.	Paracetamol	NSAID	[40]
Wamorkar et al.	Metoclopramide	Anti-emetic	[41]
Bhimani et al.	Clarithromycin	Antibiotics	[42]
Rajalakshmi et al.	Levofloxacin Hemihydrate	Anti-H. pylori	[43]
Rathod et al.	Ambroxolhydrochloride	Secretolytic agent	[44]
Patel et al.	Hydrochlorothiazide	Antihypertensive/Diuretic	[45]
Patel et al.	Famotidine	Antihistaminic	[46]
Lahoti et al.	Ofloxacin	Antibiotics	[47]
Chiprikar et al.	Acyclovir	Antiviral	[48]

Future Prospects with respect to Herbal drugs

The pharmacy industry's newest area is herbal medication distribution. The innovative method for improved delivery is the use of floating *in-situ* gel for herbal medications. For the past 20 years, pharmaceutical research professionals have focused heavily on the medication release profile. Working on GI transit profiles is a fantastic opportunity for the scientists. This has led to the development of novel products that offer patients significant advantages. With the introduction of floating *in-situ* gel, devices that can release drugs for up to 24 hours have been developed. Several herbal remedies that may be administered in floating *in-situ* gel system include: Ginger, Turmeric, Liquorice, Berberine and Black myrobalan.

CONCLUSION

Floating oral *in-situ* gels are an innovative gastro-retentive drug delivery system that form buoyant gels upon contact with gastric fluids, enabling prolonged stomach retention and sustained drug release. Triggered by physiological stimuli such as pH, temperature, or ionic changes, these systems using polymers like sodium alginate, gellan gum, and HPMC that enhance bioavailability, maintain consistent plasma levels, and minimize gastric irritation. With advantages like ease of administration, cost-effectiveness, and improved patient compliance, floating oral *in-situ* gels offer a promising approach for controlled and site-specific gastric drug delivery.

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