IJNRD.ORG ISSN : 2456-4184
INTERNATIONAL JOURNAL OF NOVEL RESEARCH AND DEVELOPMENT (IJNRD) | IJNRD.ORG
An International Open Access, Peer-reviewed, Refereed Journal

ADVANCES IN GASTRO-RETENTIVE DRUG DELIVERY: EXPLORING SUPERPOROUS HYDROGELS FOR ENHANCED DRUG RETENTION

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Abstract :

Oral route is most preferable route of administration but it has certain limitations for those drugs which absorb from specific region of gastrointestinal tract. Prolonged gastric retention improves bioavailability, reduces drug waste, and improves solubility for drugs that are less soluble in a high pH environment. Gastro retentive systems (GRDDS) are designed on the basis of delayed gastric emptying and CR principles, and are intended to restrain and localize the drug delivery device in the stomach orwithin the upper sections of the small intestine until all of the medication has been discharged.Hydrogels are becoming increasingly popular among scientists across various sectors of inquiry. Intelligent hydrogels play a crucial role in several applications. Superporous hydrogels were initially designed as a medication delivery technology to maintain dose form throughout the upper gastrointestinal tract and absorb drugs in the gastric media.Superporous hydrogels (SPHs) have been produced that exhibit rapid swelling and superabsorbent characteristics, attracting significant attention for a variety of biological applications.

KEY WORDS : Oral route, GRDDS, Superporous Hydrogels, Swelling and superabsorbent property

Introduction:

Oral medication delivery is so much easier to administer, patients are more likely to comply, the formulation can be more flexible, and other factors make it the preferred method of drug delivery. Oral dosage formulations have advanced significantly, going from instant release to site-specific delivery[1].Oral dose formulations have evolved dramatically, from rapid release to site-specific delivery, minimal medication costs, patient compliance, and formulation flexibility. Oral administration is used to administer about 90% of all medications. Solid oral dose forms are the most often used product category, even if the medications are taken orally. Drug release from the dosage form, the rate at which pharmaceuticals are absorbed in the gastrointestinal tract, the stomach emptying process, and the site of absorption all influence how differently drugs are absorbed in the GIT. Medications with short half-lives and easy absorption from the GIT are rapidly removed from the systemic circulation[2].

Drug's gastric residence time can be further extended using gastro retentive devices, which can stay in the stomach area for several hours. Gastric retention can be achieved by a number of different methods (approaches), such as flotation or buoyancy, mucoadhesion, sedimentation, expansion, and geometry[3]. Controlling the location of a DDS in a particular GI tract segment has several benefits, particularly for medications that have stability issues or show a GI tract absorption window. All things considered, close contact between DDS and the absorbing membrane may both accelerate and slow down drug absorption[4].

Microspheres are tiny, spherical particles with dimensions between 1 and 1000 µm. Microparticles is another name for microspheres and can be made from a variety of both synthetic and natural materials.Commercially available microspheres include glass, polymer, and ceramic materials. Because the densities of solid and hollow microspheres range greatly, they have diverse uses. Usually employed as additives, hollow microspheres reduce a

material's density. Floating microspheres are also referred to as hollow microspheres, micro balloons, or floating microparticles. Strictly speaking, floating microspheres are spherical, empty particles devoid of a centre. These particles move freely and range in size from 1 to 1000µm. Kawashima has used an emulsion solvent evaporation process to create non-effervescent hollow polycarbonate microspheres.This gastrointestinal transitcontrolled formulation is intended to float in gastric juice with a specifi cdensity of less than one.

This characteristic causes prolonged transit through the stomach.When microspheres come into contact with gast ric fluid, the gel formers, polysaccharides, and polymers hydrate to form a colloidal gel barrier, which regulates t he rate of fluid penetration into the device and thus drug release.The air trapped by the expanded polymer reduce s the density and provides buoyancy to the microspheres. However, a low stomach content is required to enable the right buoyancy mechanism of drug release from the microspheres[5]. However, a low stomach content is Recent research has focused on the development of Esomeprazole microspheres using enteric coated polymers, such as Eudragit L100, through the antisolvent precipitation method in order to achieve the highest drug concentration while also improving stability and bioavailability in an acidic environment. A 32 factorial design was employed to generate the Esomeprazole microsphere, with polymer quantity and rpm as variables[6].

Mucoadhesive buccal patches that release drugs into the mouth cavity at a predefined rate may offer different advantages over standard dose forms like pills, gels, and solutions. A buccal patch for systemic acyclovir administration in the oral cavity was developed using polymers hydroxy propyl methyl cellulose (K4M), hydroxy propyl methyl cellulose (K15M), sodium carboxy methyl cellulose, poly vinyl pyrrolidone (K30), polyethylene glycol (400), and a Eudragit backing membrane (RL100). The films were tested based on swelling, residence time, mucoadhesion, release, and organoleptic qualities[7].Using the solvent casting method, mucoadhesive buccal patches were created with various grades of hydroxypropyl methylcellulose (HPMC) (K4M and K100M) and polyvinylpyrrolidone-K30. The amount of the release retardant polymers, HPMC K4M (X1) and HPMC K100M (X2), served as an independent variable. The dependent variables were burst release within 30 minutes (Y1), cumulative percentage release of medication after 8 hours (Y2), and patch swelling index (Y3). In vitro release and swelling studies were carried out, and the data were fitted to kinetic models[8].

Superporous hydrogels were created as a unique drug delivery technology for medications with an absorption window in the stomach and upper gastrointestinal tract. Superporous hydrogels were created as a unique drug delivery technology for medications with an absorption window in the stomach and upper gastrointestinal tract. A superporous hydrogel is a composite polymer made from a solid hydrogel plus air. The SPH is a unique type of porous hydrogel with an average pore size of 50-100 um. Superporous hydrogels are three-dimensional networks of hydrophilic polymers that absorb a high volume of water in a short period of time. These hydrogels differ from other porous hydrogels in terms of pore diameters and methods for generating the pores[9].

Many transdermal dose forms are available, including gels, ointments, creams, and so on. Gels are solid, jelly-like materials that range in hardness and toughness. Gels are characterized as dilute cross-linked systems with no flow in steady-state conditions. Gels are further classed as hydrogels, xerogels, and organogels. Hydrogels are polymeric networks that may absorb significant amounts of water yet remain insoluble due to chemical or physical cross-linking. Hydrogels are three-dimensional network systems. is caused by the crosslinking of polymeric chains. Cross linking can occur by physical contacts, covalent bonding, hydrogen bonding, or van der wall interactions. Hydrogels are clever enough to respond to environmental variables such as pH, temperature, and ionic strength, electrostatic field and presence of enzyme[10]

Physiology of stomach

When planning a surgical resection, the four segments of the stomach—the cardia, fundus, corpus or body, and antrum—serve as crucial guidelines. The stomach's closest portion, known as the cardia, is situated right after the gastroesophageal junction. The fundus is the region of the stomach above the gastroesophageal junction.The angularis incisura, a notch on the stomach's smaller curvature close to the pyloric end, marks the corpus, or body, which is placed between the fundus and the antrum. The antrum, which is the final segment, joins the duodenum and the corpus or body at the pyloric sphincter, a thick, muscular valve.These segments each play distinct roles in the digestive process and differ histologically[11]. The stomach has two functions: storing food and assisting the small intestine with digestion and nutrient absorption. The stomach's function is controlled by various neurological and hormonal factors. The stomach produces acid, which is essential for digesting[12].

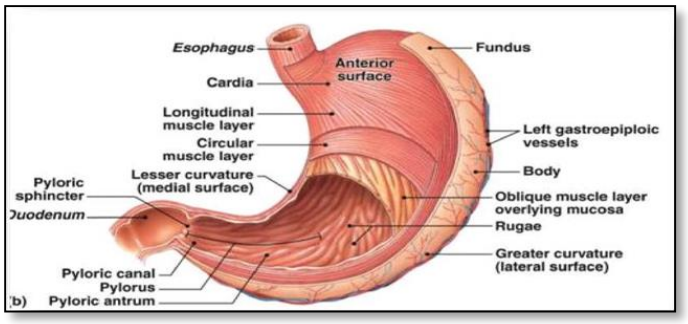

figure 1 physiology of stomach[13]

Anatomy of stomach

The alimentary canal's widest section is the stomach. It is a structure that resembles a bag that is connected with the duodenum at a distance and the abdominal oesophagus up close. The peritoneum encases the stomach. Because the proximal and distal ends of the stomach are fixed to surrounding structures, they are comparatively immobile. The stomach moves quite a bit in other places. The stomach's main jobs include: Acting as a reservoir and receptacle for food that has been consumed; Secreting hydrochloric acid and proteolytic enzymes that start the breakdown of proteins and eliminate many harmful bacteria from the food;

To churn the meal and use the stomach liquid to soften it, creating a liquefied mixture known as chyme[14].

During the fasting state, the stomach and intestine undergo an interdigestive sequence of electrical events every two to three hours. The migrating myoelectric cycle (MMC), also known as the interdigestivemyoelectric cycle, is further subdivided into the following four phases.
Base phase, or Phase I ,Thepreburst period, or period II ,The burst phase, or Phase III ,Stage IV[15].

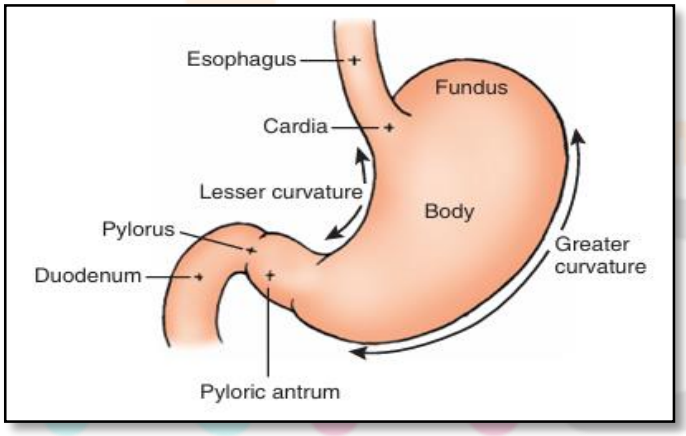

figure 2 anatomy of stomach[16].

Advantages

Extended Gastrum Retention: GRDDS increases the amount of time a medicine remains in the stomach, which is beneficial for drugs that are absorbed in the upper gastrointestinal system[17]. Improved Bioavailability: Drugs with a short window for absorption are made more bioavailable by allowing them more time to absorb in the stomach[18]. Decreased Dosing Frequency: Better patient compliance results from the regulated release of medications, which lowers the frequency of dosing[19].Localized Drug Action in the Stomach: Helicobacter pylori infection and other conditions can be treated specifically in the stomach thanks to GRDDS[20].Fit for Intestine-Degraded Drugs:

GRDDS is advantageous for medications that are stable in the intestinal environment but unstable in the stomach's acidic environment[21].

Disadvantages

Variability in stomach emptying: GRDDS effectiveness is primarily dependent on an individual's stomach motility, which varies with age, health, and diet[22].Risk of Gastric Irritation: If a medication is acidic or irritates the stomach, prolonged contact with it may cause irritation[23].Gastric fluid instability: Some medications breakdown in the stomach's acidic environment. GRDDS may be ineffective for certain medications unless additional stabilizers or protective coatings are employed, complicating the formulation and perhaps increasing costs[24].Complex Formulation and Increased Costs: The development of GRDDS requires the application of advanced formulation techniques, which may result in an increase in the production process's complexity and expense[25].Limited Applicability for Certain Patient Populations: GRDDS may not be helpful for patients with certain gastrointestinal conditions, such as gastroparesis, or those who take medications that accelerate stomach emptying[26].

Applications

Release: For medications with a limited window for absorption, GRDDS enables sustained drug release over a long period of time, boosting therapeutic results[27].Increased Bioavailability: GRDDS can improve the absorption of medications that are more readily absorbed in the gastrointestinal environment by keeping them in the stomach[28].Targeted Delivery: Certain GRDDS can be designed to deliver medications at particular GI tract locations, which makes them useful for treating disorders like stomach ulcers locally[29].Antibiotic Therapy: By preserving localized concentrations in the stomach, GRDDS can increase the efficacy of antibiotics and lower the risk of infections like H. pylori[30].Antiretroviral Drug Delivery: GRDDS can benefit some antiretroviral medications, such as lamivudine, by maintaining effective drug levels in the stomach, perhaps aiding in increased absorption and efficacy in HIV therapy[31].

Classification of polymers

Water soluble synthetic polymers

Hydrophilic functional groups such as pyrollidone, amide, or ester are present in water-soluble synthetic polymers. These polymers are frequently harmless and biocompatible. Polyethylene glycol, polyvinyl pyrollidone, polyacrylamide, and polyacrylic acid are examples of these polymers[32].

Polyacrylic acid

By joining the lengthy, linear chains in these polymerizations, the crosslinking agent—a monomer with two or more double bonds—provides the structure of the polymer network. Hydrogel networks made of poly (acrylic acid) (PAA) are the foundation of a class of materials known as super absorbents because they can absorb several times their weight in water[33]. When tested on mice's skin, the prepared griseofulvin topical hydrogels comprising PG and NMP were found to be safe, stable, and very efficacious. Permeation was shown to be statistically significant for formulations that contained both PG and NMP. This could be explained by the drug's improved solubility and partitioning from the formulations as a result of penetration enhancers[34]. Liposomes integrated into the hydrogel demonstrated their suitability as a novel vaginal delivery system with localized and sustained release of encapsulated acyclovir through in vitro release tests. Over 35% of the medication that was initially encapsulated remained in the hydrogel even after 24 hours of incubation in a vaginal fluid simulant[35].

Polyvinyl alcohol

Polyvinyl alcohol (PVA)-based hydrogels stand out for their excellent mechanical qualities and capacity to hold water in the structure, which guarantees a long-lasting moist environment, in addition to the benefits of conventional hydrogel materials (capacity to absorb water, gas permeability, soft tissue imitation, flexibility, and

biocompatibility).By alternating cycles of freezing and thawing, PVA hydrogels can be produced. The PVA material made this way is stronger mechanically than the one made with UV light as the cross-linking agent. Additionally, PVA has a wider range of applications due to its more accessible functional groups compared to the PEG structure. However, the rate and degree of degradation can be controlled by generating PVA/PEG copolymers in varying proportions: a larger PEG block concentration shortens the hydrogel degradation period[36]. To enhance the biocompatibility of pure poly(vinyl alcohol),(PVA) hydrogels, "bioartificial hydrogels" were created by combining PVA with several biological macromolecules, including gelatin, dextran, and hyaluronic acid[37].

Polyvinyl pyrrolidone (PVP)

6% in DI water, with an additional 4% K2 S2 O8. PVP/K2 S2 O8 hydrogels had a faster swelling rate, larger absorption capacity, and better BSA solution penetration into the hydrogel system than PVP hydrogels. This indicates biocompatibility with biochemical systems, appropriateness for drug release, and protein separation from plasma[36].PVP improves the mechanical stability of SPHs. When coupled with other polymers (such as acrylamide or acrylic acid), it forms an interpenetrating network that gives strength and durability, which is very beneficial in physiological settings[38].

PolyethyleneGlycol(PEG)

A wide range of cell types, including chondrocytes, fibroblasts, vascular smooth muscle cells, osteoblasts, neural precursor cells, and mesenchymal stem cells, have been encapsulated in 3D using PEG-based hydrogels. A PEG-based hydrogel technology serves as a platform for hepatic tissue creation[39]. PEG enhances the flexibility of SPHs, lowering brittleness and improving the hydrogel'smechanical characteristics, which is critical for applications where frequent deformation is required[40].

Polyacrylamide

Polyacrylamide is the most widely utilized temperature-responsive polymer due to its lower critical solution temperature (LCST) behavior, and it is commercially available. These polymers have demonstrated versatility in medicinal and electrical applications[41].

Natural polymers

Gelatin

Gelatine is a biomaterial with multiple advantages: it is bioresorbable, antigenic in physiological settings, and preserves easily modifiable physicochemical features . It also promotes immediate haemostasis, which helps to reduce wound contracture and the contour deformities associated with traditional wound healing[42]. Gelatin can improve the structural integrity of SPHs while also promoting cell adhesion, which is useful in tissue engineering scaffolds. It interacts well with other polymers, boosting hydrogel stability while maintaining its porous nature[43].

Dextran

Dextran is a natural glucose-containing polysaccharide that is an excellent starting material for hydrogel formation. The oxidation of dextran with sodium periodate is a simple and well-known process for functionalizing dextran with aldehyde moieties. Dextran hydrogels have also been utilized to stabilize and administer fibroblast growth factors for tissue control[44].

Xanthan gum

Xanthan gum (XG) is an extracellular polymer produced by the bacterium Xanthomonas campestris. The anionic nature of XG is owing to the presence of both glucuronic acid and pyruvic acid groups in the side chain. Because of its inertness and biocompatibility, XG has the potential to be an effective drug carrier. XG is commonly used as a suspending and stabilizing agent in oral and topical formulations, as well as a release enhancing agent in hydrophilic matrix tablets and pellets[45].

Hydrocolloids:

Carrageenan

Carrageenan is a natural carbohydrate (polysaccharide) derived from edible red seaweed[46].

Stimuli-responsive superporous hydrogels (SPH) are gaining popularity because to their increased pore content, which allows for greater exposure of the hydrogel to the swelling media, resulting in faster swelling kinetics. This distinguishing feature of SPH makes them particularly promising for the efficient delivery of bioactive compounds to precise target regions. The interplay of hydrogen bonds and double helix entanglement helps to maintain the system's structural integrity. The presence of −OH groups helps increase adhesion at the target region. As a result, it is appropriate for usage as a thermo-reversible gel with a high polymer volume fraction, making it an excellent candidate for a targeted controlled-release drug delivery system[47].

Alginates

Stanford originally extracted alginates from brown algae using an alkaline extraction method similar to iodine extraction[48].Sodium alginate possesses qualities that make it suitable for usage in food and products, such as the ability to retain water, gel, thicken, and form capsules and films. Furthermore, its consumption does not cause toxicity, and it is a biocompatible and human-degradable substance[49]. Alginate hydrogels can be made using a variety of cross-linking processes, and their structural closeness to extracellular matrices found in livingtissues allows for a wide range of applications, including wound healing, bioactive agent delivery (such as tiny chemical medicines and proteins), and cell transplantation[50].

Hyaluronic acid (HA)

Hyaluronic acid (HA), also known as Hyaluronan, is an anionic, non-sulfated glycosaminoglycan (GAG) that spreads widely throughout connective and epithelial tissues. Mucopolysaccharide, which is one of the major components of the extracellular matrix (ECM)[51].HA-based hydrogels with adjustable stiffness and a spatially defined microstructure. The combination of stimuli-responsive chemistries and biofabrication technologies can be utilized to customize hydrogel degradation, mechanical strength, and structural patterning for applications such as cellular behavior control and disease therapy[52].

Chitosan

Chitosan is created by deacetylating chitin, which converts certain N-acetylglucosamine moieties into glucosamine units. The presence of high numbers of protonated -NH2 groups on the chitosan structure is responsible for its solubility in acidic aqueous conditions, as its pKa value is about.Polymer viscosity is an important technological parameter because extremely viscous solutions are difficult to manage. Furthermore, viscometry is an effective instrument for estimating the molecular weight of chitosan since it is a simple and rapid method, despite the fact that it is not an absolute method and hence requires the measurement of solvent-specific constants[53].

Starch based polymer

Starch is the most abundant storage carbohydrate in plants, found as granules in the chloroplast of green leaves and the amyloplast of seeds, pulses, and tubers. Starch-based hydrogels have several advantageous qualities, such as biodegradability, hydrophilicity, biocompatibility, cheap cost, and non-toxicity[54]. The stiffness and structure of branching amylopectin chains can improve water retention capacity, hence glutinous rice starch-based SPAM (75.1% amylopectin content) had good water absorption characteristics (399 g water/g)[55].

Cellulose derivative

Cellulose and its derivatives have been shown to be adaptable materials with a unique chemical structure, making them an excellent basis for the development of hydrogel networks with different qualities such as swelling ability and sensitivity to external stimuli.
Thus, cellulose esters are water-insoluble polymers with good film-forming properties that have a wide range of applications, including classical material coatings and controled-release systems, hydrophobic matrices, and

semipermeable membranes for use in pharmacy, agriculture, and cosmetics. Furthermore, cellulose esters (e.g., cellulose acetate (CA), cellulose acetate phthalate (CAP), cellulose acetate butyrate (CAB), cellulose acetate trimelitate (CAT), hydroxypropylmethyl cellulose phthalate (HPMCP)) are widely used as binders, fillers, and laminate layers in composites and laminates, as an excellent material for photographic films, and as membrane-forming materials applicable for gas separation, water purification, food and beverage manufacturing, pharmaceutical andbioscience fields[56]

Need for super porous hydrogels

SPHs emerged to meet specific medicinal purposes, such as gastric retention. Research indicates that certain SPH formulations may be suitable for heavy-duty applications that require exceptional swelling and mechanical properties in hostile conditions. The viability of employing SPHs in oral solid and semi-solid dosage formulations has been investigated. SPH formulations have been assessed in-vivo for safety and efficacy, indicating potential for further development in pharmaceutical, food, and biological applications. Superporous hydrogels' unique features make them suitable for non-pharmaceutical and non-biomedical uses[57].

Probable candidates for super porous hydrogels

CR-GRDF is best suited for compounds with low intestinal absorption but superior absorption in the upper GIT.

Narrow therapeutic window in GIT, such as riboflavin and levodopa. Calcium supplements, chlordiazepoxide, and Cinnarizine are absorbed mostly from the stomach and upper GI tract. Drugs that act locally in the stomach, such as antacids and misoprostol. Drugs that breakdown in the colon, such as ranitidine hydrochloride and metronidazole .Drugs that disrupt typical colonic bacteria, such as amoxicillin trihydrate[58].

Methods for preparing super porous hydrogels

Homopolymer hydrogels

Cross-linked homopolymer hydrogels are commonly used in contact lens manufacture, and one method is to employ poly (2-hydroxyethyl methacrylate) as a monomer, cross-linking agent; polyethylene glycol dimethacrylate, and UV-sensitive initiator; benzoin isobutyl ether. The cross-linked film is produced in de-ionized water and then exposed to UV radiation (λ = 253.7 nm) for 20 minutes. The next step is to immerse in water for 24 hours until completely saturated and non-toxic.Polyvinyl Alcohol (PVA) hydrogels are formed through repeated freezing and thawing cycles. This form of PVA material preparation delivers more mechanical strength than UV radiation. Radiation can be used to produce polyvinylpyrrolidone (PVP) hydrogels, which are then employed in wound healing[59].The polymerization mechanisms of PEG-based hydrogels, as well as their usefulness in regenerative medicine applications, are discussed. Furthermore, the design factors that are critical in ensuring the availability and stability of the biomolecules, as well as the methods for loading biomolecules into PEG hydrogels[60].

Copolymeric hydrogels

Copolymeric hydrogels are made up of two or more distinct monomer species with at least one hydrophilic component, organized in a random, block, or alternating arrangement along the chain of the polymer network[61].There are numerous notable copolymeric hydrogels composed of suitable monomers, including poly(NVP-co-HEMA), poly(HEMA-co-MMA), and others . A tri-block comprising polyethylene glycol,

polycaprolactone, and polyethylene glycol was prepared. The mechanism of Є caprolactone copolymerization is discussed[10].

Semi interpenetrating network (Semi IPN)

In this type of hydrogel, one polymer enters the crosslinked network without forming a chemical bond. They are advantageous because of the change in pore size and delayed drug release. Semi-IPN of alginate and amine terminated poly (N-isopropyl acrylamide) PNIPAAm were produced with calcium chloride as a crosslinking agent. These hydrogels are sensitive to temperature and pH. N, N, methylenebisacrylamide is utilized as a crosslinking agent, ammonium persulfate as an initiator, and trisodium citrate as a reducing agent. The crosslinked polymer is PHEMA. Semi-IPN of gum Arabic is made by loading silver nitrate, which has strong antibacterial activity. One of the semi-IPN is the inclusion of linear cationic polyallyl ammonium chloride in acrylic or acrylamide co-polymer hydrogels[10].

Inter Penetrating Network (IPN)

IPNs are "alloys" of cross-linked polymers in which at least one is synthesized and/or cross-linked in the presence of the other, there are no covalent bonds between them, and they cannot be separated unless chemical links are broken. The polymers must be combined successfully to provide an advanced multicomponent polymeric system with a new profile .IPN hydrogels can be classified into two types based on their preparation chemistry: (i) simultaneous IPN, which occurs when the precursors of both networks are combined and the two networks are synthesized concurrently using independent, noninterfering routes such as chain and stepwise polymerization. When a linear polymer, either synthetic or biopolymer, is entrapped in a matrix, resulting in a semi-IPN hydrogel, fully-IPN can then be created via selective cross-linking of linear polymer chains[62]

Evaluation:

Swelling study

Swelling Time

This is a key feature of superporous hydrogels. The time of swelling of the hydrogel was determined by immersing it in swelling media and recording the time until equilibrium swelling. Swelling ratio First, the hydrogel was completely dried and then placed in excess of swelling medium. At a predetermined time, hydrogel was removed from the media and weighed. The swelling ratio was calculated as $Qs = Ws\text{-}Wd/Wd^{x}100$. Qs is the swelling ratio, and Ws is the weight of the hydrogel in its swollen condition. Wd - Weight of the dried hydrogel[63].

Swelling Index

Swelling tests were performed with the VankelDissolution Apparatus (VK7020S, Varian, Palo Alto, CA, USA). No rotational speeds were used. Pre-weighted tablets were immersed in 500 mL of medium (deionized water, DIW; simulated gastric solution, 0.1N HCl) for 8 hours at 37.0 ± 0.5°C. At predetermined intervals (0, 0.5, 2, 4, 6, and 8 hours), the enlarged tablets were withdrawn from the solution, cleaned with a paper towel to remove surface droplets, and weighed. The swelling index (SI) was derived using the following equation:

$$SI=Wt\text{-}Wo/Wo$$

where Wo is the dry tablet's starting weight and Wt is the swollen tablet's weight at time t. Data are reported as mean ± standard deviation (SD)[64].

Porosity measurement

Porosity measurement Porosity is a key characteristic that influences the swelling ratio, mechanical strength, and drug release profile. To determine porosity, dried SPH was immersed in hexane overnight and weighed after the excess hexane on the surface was wiped. The porosity was computed as: Porosity = VP/VT. Where VP (VT-VSPH) is SPH's pore volume and VT is its total volume. The total volume of SPHC may be calculated from its dimensions, as it is cylindrical in shape[63].

Determine the empty fraction.

The dried superporous hydrogel is immersed in 0.1 N HCl until equilibrium is achieved. The dimensional volume of the swollen hydrogel is estimated once its dimensions have been measured. Meanwhile, the amount of buffer absorbed into the hydrogels is estimated by subtracting the weight of dry SPHs from the weight of swelled hydrogels, and the resulting value is determined by the total volume of pores inside the SPHs.

[65].

Determination of drug content.

Weigh 5mg of super porous hydrogel accurately and transfer it to a 100ml volumetric flask holding 10ml of pH 1.2 0.1 N HCL. Make up to the volume. After sifting the mixture, the drug content is evaluated using UV-visible spectroscopy[66].

Degradation Kinetics

The hydrogel's breakdown kinetics are investigated by measuring the swelling ratio as a function of water retention. The hydrogel is placed in a pH 1.2 (0.1 M HCl) medium at 37°C for 12 hours, and the samples are weighed at 6-hour intervals. The water retention capacity (WRt) is calculated as a function of time using the equation below.

$$WRt = Wp\text{-}Wd/ Ws – Wd$$

where Wd is the weight of the dried hydrogel. Ws is the weight of the fully swelled hydrogel, and Wp is the weight of the hydrogel after different exposure times[63].

Mechanical characteristics.

The penetration pressure (PP) of SPHs is measured with a bench comparator. The entirely swelled hydrogel is positioned lengthwise beneath the lower touch, and weights are gradually applied to the top touch until the polymer ruptures completely. Measuring equipment can quantify compressive force, and penetration pressure can be computed as, pp=Fu/S

Fu- Compressive strength at which the polymer breaks completely.

S-Lower touch area[66].

In vitro evaluation test:

The glass beaker can accommodate 70 mL of dissolution medium (0.1 N HCl). This proposed approach mimics the stomach emptying process by placing a side arm at the bottom of the beaker . The Rossett-Rice test has a higher stir ring rate (300 rpm) than the modified dissolution test (70-75 rpm). The dissolution was agitated at 75 rpm while maintaining a temperature of 37 ± 0.5°C. 0.1 N HCl was added to the burette at a rate of 2 mL/min. The dissolution media and the dissolved medication emerged from the side arm at the bottom of the beaker. Samples of 5 mL were taken at regular intervals and promptly replaced with 5 mL of new solution medium[67].In vitro drug release tests are often performed in simulated stomach juices at 37 degrees Celsius. Due to the difference in gastric pH between fasting and fed circumstances, it is also recommended to investigate drug release profiles at somewhat higher pH, such as phosphate buffer pH 5.8 or 6.8. dissolving tests are typically performed using a USP II dissolving device[68].

FTIR analysis

The drug and excipients were investigated using Fourier transform infrared (FT-IR) technology to determine their physical and chemical interactions. The FT-IR spectra of both the pure drug and the floating tablet were acquired using the KBr mixing method on the FTIR-1700 Shimadzu FT-IR analyzer at the institute's central instrument laboratory[69], [70].

Differential Scanning Calorimetry (DSC).

Differential scanning calorimetry (DSC) The physical and chemical interactions between the medicine and its excipients were examined using DSC. The DSC spectra of pure medicines and drug composite mixes were acquired using the DSC-60 instrument, which is housed at the institute's core instrument laboratory[71].

Stability study

According to ICH Q1A (R2), new pharmacological compounds and products must undergo stability testing. The goal of rules stability testing is to determine a re-test period for the substance being tested, a shelf life for the drug product, and recommended storage settings[72].It also shows how the quality of a medicinal product or medication material changes over time as a result of numerous environmental conditions such as temperature, humidity, and light[73].Short-term stability testing of the optimal batch was carried out at 40°C in a humidity container with 75% relative humidity (RH) to determine the variation in the in vitro dissolution profile and during storage. After a month, samples were removed to see if the pattern of drug release in vitro had changed[74].

table 1 anti -diabetic drugs based on gastro retentive drug delivery system

Category of drug	Preparation method	Polymers used	Drug	References
1.Biguanides	3 D Printing	HPMC	Metformin HCL	[75]
2. Meglitinides	Quasi-emulsion solvent diffusion	HPMC Na Alginate	Mitiglinide	[76]

3. Biguanides	Direct compression floating tablet	HPMC	Metformin HCL	[77]
4. Meglitinides	Solvent diffusion-evaporation technique	Ethyl cellulose	Repaglinide	[78]
5. Biguanide	Inotropic gelation technique	Na CMC, HPMC K100M	1,1-Dimethyl biguanide	[79]

Table 2 Anti -cancer and antibiotic drugs based on Gastro retentive drug delivery system

Category of drug	Preparation method	Polymers used	Drug	References
1.Antibiotic Anti-amoebic	Semi-IPN	Freeze dried chitosen, Polyethylene oxide	Amoxicillin and Metronidazole	[80]
2.Antibiotic H_2 receptor antagonist	Solvent evaporation method	Polymethyl Methacrylate (PMMA)	Amoxicillin HCL and Nizatidine HCL	[81]
3.Antimetabolite pyrimidine antagonist	o/w emulsification solvent evaporation method	Ethyl cellulose	Capecitabine	[82]
4.III generation cephalosporin	Inotropic gelation method	HPMC K4M, HPMCK15M, Ethyl cellulose	Cefexime trihydrate	[83]
5.Fluroquinolones antibiotic	Solvent evaporation method	HPMC, Ethyl cellulose, Eudragit S100, Eudragit L100	Levorfloxacin	[84]
6.Antimetabolite Pyrimidine antagonist	Solvent diffusion evaporation method	Polyvinyl pyrrolidone, Ethyl cellulose	5-FU	[85]

Table 3 some other drugs based on Gastro retentive drug delivery system

Category of drug	Preparation method	Polymers used	Drug	References
1.β- blocker	Solvent diffusion evaporation technique	Eudragit 100(F2) cellulose acetate(F1), Acrycoat S100(F3),	Acebutalol	[86]
2.Antiviral drug	Solvent diffusion evaporation technique	Ethyl cellulose, HPMC, PVA	Acyclovir	[81]
3.NSAID	Solvent evaporation technique	Ethyl cellulose	Ibuprofen	[87]
4.Antiviral	Emulsion solvent diffusion method	HPMC,PVA	Ritonavir	[88]
5.Angiotensin II receptor blocker	Nonaqueous solvent evaporation method	PEG 4000	Telmisartan	[89]
6.PPI	Solvent evaporation method	HPMC K15M, Ethyl cellulose	Pantoprazole sodium	[90]
7.H_2receptor antagonist	Semisolid extrusion 3D Printing	HPMC,Polyvinyl pyrrolidone K30	Famotidine	[91]
8.Antiemetic (dopamine antagonist)	3-D Printing	PVA , PLA Filament	Domperidone	[92]
9.Anti-convulasant	Direct compression floating tablet	HPMC, HPC	pregabalin	[93]
10.Anti-asthmatic	Bilayer floating theophylline tablet	Eudragit RL100	Theophyllin	[94]
11. Ca channel blocker	Effervescent floating matrix system	Polyethylene oxide	Azelnidipine	[95]

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Conclusion :

Superporous hydrogels are novel and highly effective class of hydrogel material which increases drugs bioavailability, controlled release and serving as most promising device for gastro-retentive delivery. Superporoushydrogelin various pharmaceutical fields where fast swelling properties is required. A successful oral drug delivery platform that uses SPHs is expected to meet the certain criteria including safety ,effectiveness ,desirable drug loading and release.

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