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A REVIEW: SUPERPOROUS HYDROGELS

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ABSTRACT :

Superporous hydrogels were originally developed as a novel drug delivery system for those drugs having absorption window in stomach and upper part of gastrointestinal tract. These systems get swollen in the stomach immediately and in the harsh stomach environment they maintain their integrity, while the pharmaceutical active ingredient is being released. Immediate and fast swelling property of hydrogel is based on water absorption through open porous structure by capillary force. The poor mechanical strength of conventional SPHs (CSPHs) was overcome by developing the second- generation SPH composites (SPHCs) and third generation SPH hybrids (SPHHs). This review includes hydrogel, superporous hydrogel, advantages disadvantages, gastric retentive drug delivery system, different generations and drug loading techniques, characterization, application of SPHs.

Keywords: Superporous hydrogels, gastric retention, second and third generation SPH, application.

INTRODUCTION:

Drug delivery technology are very important in the pharmaceutical industries as new chemical establishments are entering, allowing successful development of a new drug as well as effective usage of existing drugs. The delivery system represents best compliance and also industrial applications. Reason establishment of hydrogels is to control the release of drug from a conventional solid dose formulation. Hydrophilic polymers are cross-linked to form a continuous network to from hydrogels. Hydrophilic polymer are cross-linked to from hydrogels. Fast swelling polymer is the more desirable; therefore, chen et al.,1999 and park developed a new kind of superabsorbent polymer so called superporous hydrogels. Swelling properties of hydrogels are mainly connected to the elasticity of the network, presence of hydrophilic functional groups (-OH, -COOH, -CONH2, -SO3H) in polymer chains, extent of cross linking, and porosity. Hydrogels are divided into conventional hydrogels and new generation depends on their swelling characteristics.

HYDROGEL DRUG DELIVERY:

There are more than 100 prescription drugs in the US, in which single excipient is commonly used, that is, hydroxypropyl methylcellulose (HPMC). Although this polymer is water soluble, it provide gelling properties when exposed to an aqueous environment. HPMC with different degrees of substitutions is use in tablet form to control the release of the drug over a longer period of time. Apparently, there are 2 features that enable the HPMC to function as a controlled delivery system. First, it is very hydrophilic due to its hydroxypropyl content. Second, the HPMC chains are in a very compressed form in a tablet, which prevent them from a fast dissolution in the aqueous environment. These 2 features provide gelling properties such as those found in a chemically cross-linked hydrogel. Although there is no chemical cross-linker in HPMC

structure, the applied pressure during tablet preparation supplies enough entanglement and barrier for the retarded dissolution of the polymer. Hydro gels are cross-linked hydrophilic polymers, with a network structure, which are able to imbibe large amount of water, and are water insoluble. For the pharmaceutical applications they are unique carriers for controlled drug delivery, release control can be governed by equally swelling and biodegrading properties. The swelling properties of hydro gels are mainly related to the elasticity of the network, the presence of hydrophilic functional groups in the polymer chains, the extent of cross-linking, and porosity of the polymer. The physical characteristics of hydro gels including their swelling ratio also depend on the balance between attractive and repulsive ionic interactions and solvent mediated effects. Owing to their high water affinity and biocompatibility, hydro gels based on poly (acrylic acid) and its derivatives, chitosan, alginate and collagen, have attracted the attention. However, these nonporous hydro gels swell slowly and exhibit low loading capacities, which restrict their effective drug delivery. A new generation of hydro gels, which swell and absorb water very rapidly, has been developed. Examples of this new generation are super porous hydro gel (SPH), which swell up to equilibrium size in a short period of time.[1-3]

Classification of hydro gels:

Hydro gels are classified as follows they are

a) Super porous hydro gels,
b) Complexation hydro gels,
c) Stimuli responsive hydro gels,
d) pH responsive hydro gels,
e) Temperature hydro gels,
f) Glucose responsive hydro gels,
g) Protein based hydro gels.

Hydrogel technical features:
The functional features of an ideal hydrogel material can be listed as follows [4]

- The highest absorption ability (maximum equilibrium swelling) in saline.
- Desired rate of absorption (preferred particle size and porosity) depending on application requirement.
- The highest absorbency under load (AUL).
- The lowest soluble content and residual monomer.
- The lowest price.
- The highest durability and stability in swelling environment and during the storage.
- The highest biodegradability without formation of poisonous species following the degradation.
- pH-neutrality after swelling in water.
- Colorlessness, odorlessness, and absolute non-toxic.
- Photo stability.
- Re-wetting capability (if required) the hydrogel has to be able to provide back the imbibed solution or to maintain it; depending on the application requirement (e.g., in agricultural or hygienic applications).

GASTRO RETENTIVE DRUG DELIVERY SYSTEM:
The most easy and preferred means of any drug delivery to the organism is oral administration. Recent incline interest in pharmaceutical field about controlled release of drug delivery through oral route have been an achievement in improving curing advantages, such as ease of dosing administration, patient compliance and formulation flexibility [5]. Drugs which are removed instantly from the systemic circulation and are easily absorbed from gastrointestinal tract (GIT) also have short lives. Suitable curing activity can be achieved by periodic dosing of drug. Release the drug slowly into the gastrointestinal tract (GIT) by oral sustained-controlled release and these formulations are an attempt to avoid this limitation and maintain drug in the systemic circulation for a long time. Such a drug would be remained and release in the stomach controlled manner so that drug could be continuously supplying to the absorption sites in the gastrointestinal

tract (GIT). There are mainly two adversities that drug delivery system suffers: the short gastric retention time (GRT) and unpredictable short gastric emptying time (GET), which can also result to incomplete drug release from the dosage in the absorption zone (stomach or upper part of small intestine) which leads to diminished efficacy of administered dose [6]. It is desirable to achieve a prolong gastric residence time by the drug delivery to formulate a sitespecific orally administered controlled release dosage. Prolonged gastric retention increases bioavailability and improves the solubility of the drug in a high pH environment [7]. It also increases the drug release duration, reduces drug waste. Prolonged gastric retention time (GRT) in the stomach could be advantageous for local action in the upper part of the small intestine e.g. treatment of peptic ulcer etc. It is an approach extend gastric residence time, by targeting site-specific drug release in the upper gastrointestinal tract (GIT) for local or systemic effect. Gastro retentive dosage forms extend the gastric retention time (GRT) for extended periods. In the past, several gastro retentive drug delivery approaches were designed and developed, including: high density (sinking) systems that is retained in the bottom of the stomach, low density (floating) systems that causes buoyancy in gastric fluid [8], mucoadhesive systems that causes bioadhesion to stomach mucosa, unfoldable, extendible, or swellable systems which limits emptying of the dosage forms through the pyloric sphincter of stomach, superporous hydrogel systems [9] magnetic system etc.

Principle of the gastric Gastric Retention of Superporous Hydrogels :

The gastric retention of superporous hydro gel is filled in a capsule so that the initial volume is small which is easy to swallow. After oral administration, it swell rapidly in the gastric fluid to a large size, so that its emptying into the intestine is prevented. When the gastric contraction reaches the hydro gel, the gastric tissues slide over the hydro gel, as it is elastic and slippery. When a drug is released from this dosage form, it slowly undergoes degradation in the stomach by either mechanical force or chemical/enzymatic hydrolysis of the polymer chains constituting the hydro gel. Eventually, the degraded super porous hydro gel dosage form is eliminated from the stomach.

Requirements for Gastric Retention of Super porous Hydro gels for Drug Delivery:

Practically for use in oral drug delivery the super porous hydro gels must have the following properties. The size should be small enough for easy swallowing. Hard gelatin capsules with size 000 are used to enclose the super porous hydro gel dosage form. The size of the swollen gel should be large enough to be retained in the stomach. The diameter of the pyloric sphincter is about 2 cm and it remains closed under normal conditions in humans. However, it could be stretched and can pass an object large than 2 cm. The swollen gel should be strong enough to withstand the peristaltic contraction. The maximal stomach contraction pressure is about 50-70 cm water pressure in humans. This number, however, reflects only the direct compression pressure. Abrasion and shear forces are also present in the stomach .Hence, to maintain the super porous hydro gel as an integral dosage form; it must be able to withstand much higher pressure than the 50-70 cm water pressure. To be applicable in humans as a drug delivery vehicle, a super porous hydro gel dosage form should be eliminated from the stomach after drugs are released. This can be obtained by either mechanical degradation to break the dosage form into small pieces or by chemical or enzymatic degradation by including biodegradable cross linkers, like glycidyl acrylate modified albumin.[2]

Advantages:

1. Enhanced patient compliance.
2. Reduced dosage frequency.
3. Buoyancy leads to improved GRT (Gastric residence time).
4. Targeted drug delivery to stomach can be achieve.
5. Increased BA and fluctuation in blood drug concentration is avoid.
6. Uniform drug release from dosage form and no possibility of dose dumping.
7. Sustained effect lead to prevention of mucosal irritation.

Disadvantages:

1. Drugs unstable & insoluble in mucosal fluid cannot be administered as GRDDS.
2. Drugs causing gastric irritation cannot be administer via this route.
3. This system require fed state to extend gastric emptying.
4. Not suitable for drugs undergo FPM (first pass-metabolism)
5. Gastric retention can be influenced by various factors which can never be constant all the time; these factors are variable & unavoidable

SUPERPOROUS HYDROGELS:

In 1999, superporous hydrogels were introduced. A superporous hydrogel is a composite polymer prepared of a solid hydrogel and air. The SPH is a unique class of porous hydrogels with an average pore size of 50-100 um. Superporous hydrogels are a three-dimensional network of hydrophilic polymers that absorb a large amount of water in a very short period of time. These hydrogels are distinguished from other porous hydrogels in the terms of their pore sizes and methods to generate the pores. Pores inside hydrogel are connected to form open channel system as capillary. Swelling of superporous hydrogels is complete by capillary wetting rather than by diffusion. Thereby, Superporous hydrogels swell completely within minutes regardless of their size due to absorption of water by capillary force rather than by easy absorption. Second generation Superporous hydrogel composites are developed which shows fast swelling, medium swelling ratio and improved mechanical properties, while third generation superporous hydrogel hybrid possess high elastic properties. From present 13C NMR studies show structure of superporous hydrogel consists of a sequence of acrylic acid (AA) and acrylamide (AM) as long aliphatic chains, which are cross-linked with N, N0 methylenebis acrylamide (Bis). Superporous structure induced by CO2 formation then stabilized by cellulosic fibers (Ac- Di-Sol) which are responsible for a delayed but also complete swelling of these superporous hydrogel composites.[10-13]

Advantages of Superporous Hydrogel [15]

1. Regardless of the size of the dried superporous hydrogel, they swell completely within a minute.
2. When it is swollen, its weight is higher than dried state.
3. They exert significant expansion force during swelling.
4. To minimize their rupture, these can be made elastic.
5. Can also be used for non pharmaceutical and non-biomedical applications.[14]

Disadvantage:

1. Weak mechanical properties of fully enlarged SPHs as compared to SPHCs and SPHHs.

Classification:-

1. First generation SPH
2. Second generation SPH
3. Third generation SPH

1. **First generation SPH (Conventional SPHs, CSPHs):-**
   The first time in 2000, Chen prepared superporous hydrogel with fast swelling and super absorptive properties. The first generation conventional SPHs (CSPH) are characterized by fast swelling, high swelling ratio and weak mechanical properties. The most commonly used monomers for the synthesis of the first generation SPHs are highly hydrophilic acrylamide, salts of acrylic acid and sulfopropyl acrylate.[16] When the SPHs are dried, the porous structure become collapsed or shrunken due to the surface tension of water pulling the polymer chains a together during the drying process. To avoid this problem, water inside the SPH is replaced with alcohol (e.g. ethanol). The small surface tension of alcohol prevents the porous structure from collapsing during drying. The dried SPHs are hard and brittle, but the hydrophilic nature of the polymer a results in moisture induced plasticization of the rigid structures into soft and flexible structures. The dried SPHs swell fast to a larger size, larger than a few hundred times of their own volume in the dried state. The rate of water absorption could be increased by creating the pores inside the hydrogel structure. Different wetting agents also increase the rate of water absorption to less than a minute. The swollen SPHs are difficult to handle without breaking due to their poor mechanical strength. An example of conventional SPH is acrylic acid and acrylamide cross-linked and polymerized on PEG acrylate substrate. [17-20]

2. Second generation SPH (SPH composite, SPHCs) :-

The second generation SPH composites (SPHC) are characterized by fast swelling, medium swelling ratio and improved mechanical properties. For making SPH composites, a matrix swelling additive or swellable filler or a composite agent is used. A composite is a matrix of a continuous phase having a dispersed phase incorporated in it. [21] A composite agent used in SPH composites is a cross-linked water-absorbent hydrophilic polymer that can absorb the solution of monomer, cross-linker, initiator and remaining components of the SPH synthesis. During the polymerization process, each swellable filler particles act as an isolated individual reactor in which polymerization and cross-linking could occur simultaneously. Since, crosslinking polymerization proceeds throughout the solution, the individual swollen particles are connected together through the extended polymeric chains. The presence of composite agent in SPH composites results in improved mechanical properties over conventional SPH, but the SPH composites are still brittle and thus break into pieces upon application of stresses. This modification over conventional SPHs resembles modification of superabsorbent polymer through surface cross-linking. Overall, this type of modification results in a higher modulus polymer network in the swollen state, which is susceptible to the failure under the brittle fracture mechanism. The most widely use composite agents are crosslinked sodium carboxymethylcellulose (Ac-Di-Sol), crosslinked sodium starch glycolate (Primojel) and crosslinked polyvinylpyrrolidone (Crosspovidone). Polyvinyl alcohol and carbopol are also used to improve the mechanical strength of SPHs. The second generation SPHs is an attractive approach for peroral and intestinal drug delivery system. Although this modification leads to polymeric networks with improved mechanical strength in swollen state but still these are prone to breakdown under high tensile stress. SPH composite can withstand compression forces of up to 2 N. [22-24]

3. **Third generation SPH (SPH hybrid SPHHs):-**

In 2003 Hossein Omidian prepared superporous hydrogel hybrid using acrylamide, methylene bisacryl amide as monomer and cross linker. They have very high mechanical or elastic properties. The third generation SPH hybrids (SPHH) are characterized by very high mechanical or elastic properties. Due to addition of hybrid agent a cross linked structure of SPH was formed. The hybrid agent is a water-soluble or water-dispersible polymer that can form crosslinked structure (in a manner similar to forming interpenetrating network (IPN) through chemical or physical cross-linking. [25,27,35] Due to interpenetrating network, SPH hybrids are also known as SPH-IPNs. Each hybrid agent may require specific treatment. Depending on the type of agent and its associated treatment, various third generation SPHs can be created ranging from high modulus to high elastic and rubber (in their water swollen states). Examples of hybrid agents are polysaccharides, sodium alginate, pectin, chitosan or synthetic water-soluble hydrophilic polymers such as poly(vinyl alcohol). Natural hydrocolloid show ionotropic gelation via treatment with metal ion like calcium, iron etc. (e.g. sodium alginate with Ca+2 ions, chitosan with phosphates). One of the unique properties of SPH hybrids is that the gels are highly elastic in swollen state. As compares with conventional SPHs and SPH composites, SPH hybrids are not easily breakable when stretched. The elastic and rubber properties make SPH hybrids a choice for various applications where resilient gels are preferred. SPH hybrids can oppose various types of stresses, including tension, compression, bending and twisting. An example of SPH hybrids is the synthesis of acrylamide based SPH in the presence of sodium alginate. SPH hybrid of alginate polyacrylamide could withstand compression forces of up to 25 N. [28, 29]

General features of various SPHs generations are listed in Table 1. [30]

Formulation	CSPH	SPHC	SPHH
Property modifier	None	Superdisintegrantscrosslinked CMC; polyvinyl pyrilidone and starch glycolate	Water–soluble CMC, alginate,chitosan, polyvinyl alcohol
Crosslinker	Diacrylate, bisAAm	Diacrylate,bisAAm	Higher MW acrylates
Inhibitor	Persulfate/diamine; water soluble azo	Persulfate/diamine	Persulfate/diamine
Swelling capacity	100-300 g g-1	100-300 g g-1	Up to about 50 g g-1
Swelling rate	5-30 s	5-30 s	5s to a few min
Mechanical properties	No mechanical strength	Resists up to 2 N cm2	Resists up to 20-100Ncm-2
Treating agent	No	No	Iron, calcium, aluminium, phosphate, copper
Water washing ability	Impractical because of high swelling in Water	Very difficult, because of high swelling in water	Readily possible because of high strength and low swelling.
Dehydration	Alcohol	Alcohol	Alcohol
Drying	Forced and vacuum	Forced/vacuum and freeze drying	Forced/vacuum and freeze drying
Physical appearance in dried state	Rigid brittle	Rigid brittle	Rigid brittle
Application	General when high and fast swelling but no mechanical properties are required	Peroral intestinal absorption of peptides; superdisintegrant	Orally administrable swellable drug delivery system.
Characterization	Fast swelling and weak mechanical properties; moisture induced plasticization, fragile against bending, compression and tensile stresses	Fast swelling, and improved mechanical properties, moisture induced plasticization, higher modulus networks fail under brittle fracture mechanism	Fast swelling and improved mechanical properties, moisture induced plasticization, highly elastic in swollen state very resistant against different stresses, ductile fracture mechanism

Method of Preparation of Superporous Hydrogel:-

Porous hydrogels are prepared using freeze drying, porogenation microemulsion formation, phase separation foaming technique, emulsion-template synthesis, and particulate leaching.

But superporous hydrogels are prepared by four methods explain below.

1. Porosigen Technique
2. Phase separation technique
3. Cross linking technique
4. Gas blowing technique

1. Porosigen Technique:-

In Porosigen Technique porous hydrogels are prepared in presence of dispersed water soluble porosigen. To prepare SPH various porosigen are used. These porosigen are hydrophilic in nature [31]. The pore size produced in the hydrogel depends on the size of porosigns. [32]

2. Phase separation technique:-

Phase separation is very critical process in generating superporous hydrogel. In solution polymerization, monomers are usually mixed in diluent that is good for both monomers and polymers. In addition, there is no control over the porosity of the gels when prepared by phase separation [10].

3. Cross linking technique:-

Crosslinking of every particle of hydrogel particles lead to aggregates of particles. The pores in these structures are present in between hydrogel particles. The size of pores are tiny than the size of particles. Individual hydrogel particles can be cross linked to foam cross linked aggregates. This technique is limited to absorbent particles with chemically active functional groups on surface [33].

4. Gas blowing technique:-

In this technique initially monomers, cross linking agent, foam stabilizer and distilled water are added in a test tube of specific dimensions pH adjust 5 to 6 with 5M NaOH [32]. The gas blowing technology has been widely used in the preparation of plastic foams from materials such as Polyurethanes, rubber, and poly (vinyl chloride). The main ingredient in the foaming process is a blowing agent (or foaming agent), which is defined as any substance or combination of substances capable of producing cellular structure within a polymer matrix [31]. After synthesis, superporous hydrogels are subjected to washing and drying.

Ingredients Required For Preparing Superporous Hydrogel [10,31]

The ingredients required for preparing superporous hydrogel are as shown in Table-2

Table-2 Role of ingredients with their examples.

Role of ingredients	Examples
Monomer	Acrylic Acid(AA),Acrylamide(AM), 3-Sulphopropyl acrylate potassium(SPAK),Hydroxy ethylmetyl acrylate (HEMA),Nisopropyl acrylamide (NIPAM), Acrlonitrile (AN), Polyviny alcohol(PVA)
Cross linking agents	**Chemical cross linker:** Glutaraldehyde,N,N-methylenebisacrylamide (BIS) **Ionotrpic cross linker:** Metal ions like calcium, iron and phosphorus
Foam stabilizers	Pluronic F127,Pluronic P105,Silwet L7605,Span,Tween
Polymerization initiator pairs	APS/TEMED(Ammonium persulfate /N,N,N,Ntetramethylenediamine, KPS/Sodium metabisulfite, APS/ Sodium metabisulfite, Azo-initiator(V545)
Foaming agents	Sodium bicarbonate, Sodium carbonate, Potassium bicarbonate
Composite agents	Crosslinked sodium carboxy methylcellulose(Ac-Di-Sol), Crosslinked sodium starch glycolate(Primojel), and Crosslinked polvinylpyrrolidone (crospovidone), Carbopol, Polyviny alcohol(PVA)
Hybrid agents	**Natural polymers:** Sodium alginate, Sodium carboxy methylcellulose (Na CMC), Chitosan based on ionotropic gelation, Pectin **Synthetic polymers:** Poly vinyl alcohol(PVA) based on cryogelation

Drug Loading into Superporous Hydrogel

Two techniques are reporyed for loading the drug into this superporous hydrogel delivery system

1. Drug loading into superporous hydrogel reservoir devices
2. Drug loading into superporous hydrogel polymers

Drug loading into superporous hydrogel reservoir devices:-

Superporous hydrogel can act as reservoir devices for drug delivery systems. There are two

1. Core inside shuttle system
2. Core attached to surface of shuttle system

These system involve two components: a core and a conveyor system. Core is the part which contains drug blend with appropriate excipients and conveyor is made up of SPH and SPHC.[34,35]

Core inside the shuttle system

Core is prepared in two different forms viz. micro particles and gross mass.[37] Micro particles are prepared by dispersing the drug in melted polymers like PEG 6000 and cooling of the mixture to get gross mass. This gross mass is crushed in mortar and sieved through mesh size #400 µm, which are used as core material. SPHC is use as body of the conveyor system because of its greater mechanical strength and SPH is used as the cap of the conveyor system because of its high swelling ratio.[26] A hole is made inside SPHC in its swollen state by use of borer, as the core has to be incorporated inside SPHC. The Superporous hydrogel composites is then dried by either at ambient temperature or by reduced pressure at 60°C.

Core attached to surface of shuttle system

In this system, core is in the form of small tablets which are prepared by dispersing the drug in melted polymer like PEG 6000 and sieving the mass through mesh size # 400 µm, which were mixed with magnesium stearate and compressed into tablets using single punch machine (40 N hardness).Conveyor is made up with superporous hydrogel composites in which two holes are made on counter side. Core tablet is placed inside the hole using bio-adhesive (cyanoacrylate) glue. Polymer swells when come in contact with gastric fluids and size of holes is enlarged. Glue help to keep the dosage forms at the site of drug absorption. same assembly is placed into gelatin capsule shells of size 000.[32]

Drug loading into superporous hydrogel polymers

The amount of water required for complete swelling of specific weights of SPH and SPHHC is determined. Drug is prepared using aqueous solution in previously determined amount of water and weighed amount of polymer is placed in drug solution to suck up the drug solution. After 20 min, completely swollen polymers loaded with drug are placed in oven at 30°C for drying overnight.[36]

Drying of SPH:-

Drying of SPH can be carried out under two different conditions.

Under condition I, swollen SPH are dried under blowing warm air (60°C) for a day in a food dehydrator.

Under condition II, swollen SPH are applied with 5–10 ml of absolute ethanol per each gel to dehydrate.

Further, SPH are dehydrated by placing them in a 50 mL of absolute ethanol several times to ensure replacement of all the water by ethanol. During this dehydration process, the soft and flexible SPH become hard and brittle. When the dehydration is completed, the excess ethanol from dehydrated SPH is removed by draining using paper towel and dried in an oven at 55°C for a day [40].

Characterization of Superporous Hydrogel:-

1) **Measurement of Density**

It was difficult to measure the density of SPH directly. The apparent density of is determined by solvent displacement method [41]. Mass of SPH is measured and then placed in a graduated cylinder containing measured volume of absolute hexane [42].

Density is calculated as follows.

Density = MSPH / VSPH

where,
MSPH: Mass of SPH
VSPH: Volume of SPH

2) Porosity Measurement

Solvent replacement method was used for porosity measurement [31,43]. Dehydrated hydrogels were immersed overnight in absolute ethanol and weighed after excess ethanol on the surface was blotted. The porosity was calculated from the following equation:

Porosity = (M2 - M1/ρV)

Where,

M1 and M2 are the mass of the hydrogel after and before immersion in absolute ethanol, respectively;
ρ is the density of absolute ethanol
V is the volume of the hydrogel [10,14].

3) Measurement of Gelation Kinetics

As the polymerization reaction proceeded, the viscosity continuously increased the full network structure (gel structure) was formed. The gelation time was defined as a period of time for gel formation following addition of glyoxal and measured by a easy tilting method after adjustment of pH to 5.0 with acetic acid. It was determined by the duration of time taken by the reactant mixture to become viscous and the viscous solution no longer descended in the tilted tube position [11,31]

4) Swelling Studies [43,44,45]

Completely dried, pre-weighed, disc-shaped SPH was weighed and then immersed in excess of swelling medium. At various time intervals, the hydrogel was removed from the solution and weighed after unnecessary solution on the surface was blotted. Results were calculated according to the following equation:

$$Q = (Ms - Md)/Md$$

Where,

Q is the swelling ratio,
Ms the mass in the swollen state and
M the mass in the dried state.

5) Determination of Drug Content

A weight of SPH containing drug in 100 ml volumetric flask was treated with about 10 ml hydrochloric acid solution of pH 1.2 mixed well and made up to volume [43]. The mixture was filtered and drug content was determined using UV-VIS spectrophotometer [31,45].

6) Mechanical Properties

The compressive strengths of various SPH formulations were determined using a bench comparator Briefly, after the fully swollen hydrogel was put longitudinally under the lower touch of a bench comparator, different scale loads were successively applied on the upper touch until the point where the hydrogel could not support any more weight and completely cracked. The pressure at this point was defined as the penetration pressure (PP) and calculated by the following equation:

$$PP = Fu/S$$

Where,

F u is that ultimate compressive force at complete breakage of polymer
S is the contact area of the lower touch [10,43]

7) Morphological Analysis

7.1) Scanning electron microscopy

The dried SPH were used for scanning electron microscopy (SEM) studies to determine the morphology of the dry samples . A JEOL JSM-840 scanning electron microscope (Jeol USA, Inc., Peabody, MA) was used after coating the samples with gold using Hummer Sputter Coater (Technics, Ltd.). Images were captured using a digital capture card and Digital Scan Generator 1 (JEOL) [45].

7.2) FT-IR spectroscopy

FT-IR spectroscopy was employed to ascertain the compatibility between the drug and polymers. It was also used to study the chemical structure of the synthesized hydrogels. The FTIR spectrum was recorded over the range of 400–4000 cm−1 [10] using KBr pellet method by Fourier-Transform Infrared (FT-IR) spectrophotometer, (Shimadzu, FT- IR 8400S, Japan).

8) Drug Loading

The method of soaking otherwise equilibration was employed for drug loading. In this method the amount of buffer necessary for complete swelling of SPH was determined. Thereafter drug solution in the determined amount of buffer which was required for complete swelling was prepared. Subsequently, SPH was placed in the drug solution and left until all the drug solution was sucked up. Then the completely swollen SPH loaded with the drug was placed in an oven at 30°C overnight [46].

9) Stability Studies

The prepared batches are kept in airtight containers and stored in stability chamber at 40°C/75%RH for three months. Results for in vitro dissolution studies obtained after three months are compared with the data obtained at the time of preparation.

10) Determination of Void Fraction

The void fraction inside superporous hydrogels was determined by immersing hydrogels in HCl solution (pH 1.2) up to equilibrium swelling. The dimensions of the swollen hydrogels were measured and by using the data, sample volumes were determined as the dimensional volume. In the meantime, the quantity of absorbed buffer into the hydrogels was determined by subtracting the weight of dried hydrogel from the weight of swollen hydrogel and the resulting values were assign as the total volume of pores in the hydrogels. Void fraction is calculated by the formula [47,48].

$$\text{Void fraction} = \frac{\text{Dimensional volume of hydrogel}}{\text{The total volume of pores}}$$

11) Evaluation of Degradation Kinetics

The degradation kinetics of the hydrogel is examined by measuring the swelling ratio as a function of water retention. The hydrogel are placed in pH 1.2 (0.1 M HCl) medium at 37°C for 12 h, and the samples are periodically weighed at 6 h interval. Water retention capacity (WRt) as a function of time is assessed as in equation.

$$WRt = (Wp - Wd|Ws - Wd)$$

where,

Wd is the weight of the dried hydrogel

Ws the weight of the fully swollen hydrogel

Wp the weight of the hydrogel at various exposure times.

12) In vitro Release Studies

In vitro drug release from the superporous hydrogels was evaluated using a United States Pharmacopoeia (USP) Dissolution Test Apparatus Type II (paddle method) [31]. At regular time intervals, samples of the dissolution medium were withdrawn, replaced with an equivalent volume of fresh dissolution fluid and analyzed for the drug using a UV-Vis spectrophotometer [43].

Application :-

1. **Gastroretentive Tablets**

   Superporous hydrogel particles of acrylic acid /sulfopropyl acrylate copolymers are mixed with gelatin and tannic acid then tableted by direct compression. Formation of hydrogen bond between gelatin and tannic acid, as well as carboxyl groups on polymeric carrier, produce an integrated matrix, which is stable after swelling. Gastroretentive tablet can swell up to 22 times its own volume within a 40 min.[39,49]

2. **Fast-Dissolving Tablets**
Methods used to prepare fast-melting tablets are freezedrying, sublimation and direct compression. First two methods prepare tablets that dissolve within 5–15 seconds. Tablets prepared by direct compression using superporous hydrogel micro particles disintegrate less than 10 sec.[30,50]

3. **Sustained Drug Delivery**
Gastroretentive system is most beneficial for drugs that act locally in stomach (antacids, antibiotics). Controlled release is improving bioavailability of drugs with narrow absorption window (riboflavin, levodopa). These systems have a bulk density of less than one so they are floating on gastric contents or relatively large in size so that cannot pass through pyloric opening. As swelling properties of both superporous hydrogel and composite are ph-dependent, these can be used as pH-sensitive drug delivery systems.[30,51,52]

4. **Diet Aid**
Superporous hydrogels can occupy significant portion of stomach space leaving less space for food, there suppressing appetite. This can help to lose weight in fat people. Maintaining integrity and volume of swollen superporous hydrogel is major challenge in use of weight loss aid.[50,53]

5. **Chemoembolization**
Chemoembolization is combined method of embolization and chemotherapy. Embolization is use in the treatment of cancer by restricting oxygen provide to growing tumours. A chemotherapeutic agent and anti-angiogenic agent can be loaded into Superporous hydrogels for chemoembolization therapy. The strong Superporous hydrogels are better candidates for this application.[14,30]

6. **Site-Specific Drug Delivery**
Riboflavin and furosemide are absorbed from stomach or proximal part of small intestine. A bilayer-floating capsule was developed for local delivery of misoprostol. By targeting slow delivery of misoprostol to stomach desired therapeutic levels could be achieved and drug waste could be reduced. HEMA based pH sensitive polymeric network has been reported as self regulated device for insulin delivery (Klumb and Horbett 1992).[14,54]

7. **Peroral Peptide Delivery Systems**
The feasibility of using Conventional Superporous hydrogels and Composites for peroral peptide delivery has been investigated. They are designed to swell in intestine with Superporous hydrogels physically adhering to gut wall and delivering incorporated peptide directly to the site.[50]

8. **Occlusion Devices for Aneurysum**
In the treatment of aneurysms Superporous hydrogels is used. Smaller size hydrogels devices prepare and placed at the aneurysm site, which quickly swells to occupy full space and form blood clot. Deposition of superporous hydrogels can result in up to 95% aneurysm occlusion without any evidence of parent artery compromise and inflammatory response. A new occlusion device prepared by combination of superporous hydrogel and platinum coils, called as Hydrocoil.[50,53]

9. **Novel drug delivery**
Here we found a platform scaffold technology that would be further examined for tissue engineering application. Superporous hydrogels composites based on aqueous Carbopol solution are good candidate for transmucosal drug delivery system. With superporous hydrogel selfnano emulsifying drug delivery system was formulate which contain containing carvedilol. Superporous hydrogels may be use as solid carrier in pharmaceutical field.[55,56]

10. **Other Applications**
Used of Superporous hydrogels other than pharmaceutical and biomedical are sanitary products, agriculture, bioseparation, enhanced oil recovery, hygiene, Diaper, horticulture, pet, colored Superporous hydrogels in decoration. Superporous hydrogels may be suitable substitute for silica

gel. High swelling pressure of Superporous hydrogels can be used to trigger an alarm system upon penetration of water.[55,57]

Table 3. Literature survey of Research involving superporous hydrogels

S.No	Drug	Rout of adminstration	Polymer	Method of preparation	Purpose
1	Atenolol [58]	Oral route	Chitosan/polyvinyl alcohol	Gas blowing method	Antihypertensive
2	Rosiglitazone [59]	Oral route	Sodium carboxy methyl cellulose chitosan	Gas blowing technique	Treat type 2 diabetes
3	Metformin [60]	Oral route	Chitosan	Gas blowing technique	Treat type 2 diabetes
4	Carvedilol [56]	Oral route	Hydroxypropyl methyl cellulose	Gas blowing technique	Antihypertensive
5	Pantoprazole [61]	Oral route	Eudragit L100	Gas blowing technique	Anti-ulcer drug
6	Amoxicillin [62]	Oral route	Chitosan	Gas blowing technique	Antibiotic

CONCLUSION:

Superporous hydrogels are a new class of hydrogel materials that swell to larger size regardless to their size and serves as a promising device for gastro retentive delivery. different generations of superporous hydrogels are investigated successfully for gastric retention. Superporous hydrogel in various pharmaceutical fields where fast swelling property is the required. Superporous hydrogel can be use as a drug carrier in the biomedical application.

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