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SYNTHESIS AND CHARACTERIZATION OF PVA BASED POLY (ACRYLIC ACID - CO - ACRYLAMIDE) SUPER POROUS HYDROGELS COMPOSITES

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Superporous hydrogels, Gas fanning approach, Polyvinyl alcohol, Bunion studies, Mechanical strength

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ABSTRACT: The aspiration of the coeval cramming is connate with the entirety of second generation Super Porous Hydrogel Composites (SPHCs) with polyvinyl alcohol as a melded material. Conglomerates were unified by proving gas fanning approach. For coalescence, 50% Acrylamide solution (AM) and 50% Acrylic Acid solution (AA) were used as a monomer, 2.5% N, N'methylene bisacrylamide (BIS) as a cross linker, 20% Ammonium Per Sulphate (APS) and 20% N, N, N', N'- Tetramethylethylene Diamine (TEMED) as a polymerization assailant pair, 10% span 80 as a foam stabilizer were used. The gaffed super porous hydrogel's were peg by inchoate enormity, computation of plausible density, porosity, bunion studies, void fraction, mechanical strength and surface morphology muse. In bifold distilled water, SPHCs trot out appalling accretion in their stasis bunion capacity. PVA revamp the bruise characteristics in twain the swelling media. SPHCs disport enriched mechanical clout as the concentration of polyvinyl alcohol is elevated. SEM images precisely marked the formation of interconnected pore, capillary channels, and the cross-linked polyvinyl alcohol molecules were espied encompassing the ambit of pores. From the characterization it was proved that polyvinyl alcohol has the good swelling properties in the synthesis of super porous hydrogel based drug delivery systems.

INTRODUCTION: The foresee of a drug at particular site has become the influential part of pharmaceutical research in contempt epoch. Howbeit discrete contentions have been beheld while covet of drug molecule at sole sites such like swift riddance, decadence and curtate residence time.



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Over the elapsed scant decades, target has been made to astute a device that can deter in the loftier section of the Gastro Intestinal Tract (GIT) in accord to reinforce the drug condo span at targeting sites.

So far there are various technologies which have been used for gastro-retentive device such as low-density systems ¹, high density systems ², bio-adhesive systems ³ and expanding systems ⁴, but these methods of approaches are affected by various factors such as gastric fluid contents, harsh gastric environment, gastric contraction and food content. Conjointly These Makin's results in paring down the gastric confinement span.

Many researchers designed hydrogel stationed GRDDS as a gastric detention expedient. As they possess hydrophilic functional group in their structure, they have the attribute to absorb considerable amounts of water and swell. A for mentioned contusion property is at the helm to pile the formulation in gut for unfurled vicinity. Thus and thus the porous hydrogels were gaffed on the basis of rad bunion and cursory acreages. A SPH is a three-dimensional plexus of a hydrophilic polymer which osmoses ample peck of water ⁵, in a mere curt aeon and their plenary blister cop in fewer than 30 sec. The gastric retention of super porous hydrogels hinge on their agile bruise property. There upon the oral administration, it ripple full tilt in the gastric fluids to a bulkier stature and hence its decant into the intestine is halted. The gastric wall drift on to the hydrogel when the gastric shrivelling ambit it.

As it is elastic, slippery and possess high mechanical strength it can able to withstand gastric contraction and besides of this it has low density and can able to float in gastric content and releases the drug in upper part of GIT. The hydrogel defer derogation in the gut either by mechanical force or chemical/enzymatic hydrolysis of the polymer chains hindmost the drug is unanimously released from the dosage form and it slowly embody the hydrogel. Sooner or later, the depraved super porous hydrogel dosage form is evicted from the stomach.

A matrix-swelling additive or a melded agent is bestow for forging SPH composites. conglomerate agent which is used in SPH composites is a cross-linked water-absorbent hydrophilic polymer which can imbibe the solution of monomer, cross-linker, initiator and tarrying constituents of the SPH entirety. The burble of SPHs is then herded by the synergy of acids and carbonates. For an instance, acetic acrylic and hydrochloric acids are frequently worn onward sodium, potassium and ammonium carbonates. Since the acid-carbonate synergy is emphatic alone in aqueous medium, the solution modus is the uttermost favoured method of polymerization in the procurement of SPHs ^{6, 7, 8, 9,} . These super porous hydrogels have found applications in biomedical and biotechnology 11 enzymes and proteins ¹³, antibiotics and antigens ¹⁴ and matrices for drug delivery systems. The equitable for the rampant inquest was to integrate SPHCs containing polyvinyl alcohol as a blended material to amend the aspect of CSPHs. Acrylic acid and acryl amide were chosen as the base monomers for their high affinity to water and faster copolymerization velocity.

While polyvinyl alcohol was selected as the second polymer component for its biocompatibility, and composites water solubility. SPH monomer, cross-linker, initiating system and watersoluble foaming additives in addition to this it have a swellable filler which acts as an isolated individual reactor, in which polymerization and cross-linking could occur simultaneously. The distended particles would then be allied to one another through the protracted polymeric chains. Upon drying, an interpenetrated network structure would be formed. Super Porous Hydrogel Composites (SPHCs) are based on polyvinyl alcohol, as the second generation SPHs, which further resulted in the improvement of properties of SPH.

MATERIALS AND METHODS:

Materials: Acrylic acid, Acrylamide, N,N. methylenebisacrylamide, span 80, ammonium persulphate, and N, N, N, N.-tetramethylethylenediamine, polyvinyl alcohol were purchased from BMR chemicals, Hyderabad, India. Double Distilled Water (DDW) was prepared in laboratory. All other chemicals used were of analytical grade and used as obtained.

Preparation of the Plain Superporous Hydrogel Composite (SPHC): 15, 16 All innards barring sodium bicarbonate were used as solution in DDW. The pH of the monomer solutions was redress to 5.5 with 5 M sodium hydroxide solution. When the pH of the monomer solution was pared down than 5, formation of carbon dioxide took place before the polymerization commences and no pores were forged inside the synthesized SPHCs. For the synthesis of SPHC of poly (acrylic acid - co - acrylamide), the following substances were added subsequently into a test tube at room temperature: acrylamide 50%; acrylic acid 50%; methylene-bisacrylamide 2.5%; span 80 10%; ammonium persulphate 20%; tetramethylethylenediamine 20%;

including soft contact lenses 12 immobilization of

poly vinyl alcohol and 200 mg of sodium bicarbonate as shown in **Table 1**. In this manoeuvre, polymerization was a vow to uphold for proximately 10 min.

In the rear, tot each innards to the test tube, the reaction amalgam was robustly rattled. Inexorably, sodium bicarbonate was farther very hastily to the solution and assimilated with a spatula. The polymerization had heretofore been evoked by ammonium per-sulphate as initiator If sodium bicarbonate was not combined fleetly bounteous, nether this riff, a few clamps were formed

furthermore and kindred SPHC polymer was not attain. Ensuing the synthesis of SPHCs, they were excised with the forceps, and concede to dry in oven at 60 °C for 48 h, and kerf into iota of imperative stature. Then the SPHC was immersed in hexane. This regimen dehydrates the SPHCs swiftly conjointly proffer shrivel. Thereafter, the SPHCs were extirpate with forceps and rivet in an oven at 60 °C for 48 h in order to ensure that the SPHCs have been dehydrated wholly. These SPHCs were hoarded in an airtight caisson prior to further avail.

TABLE 1: SYNTHESIS OF SUPERPOROUS HYDROGEL COMPOSITES

Ingredients	SP1	SP2	SP 3	SP4	SP5
[AM] (50% w/v)	300 µl				
[AA] (50% v/v)	200 μ1	200 μ1	200 μl	200 μ1	200 μ1
[BIS] $(2.5\% \text{ w/v})$	70 μl	70 µl	70 µl	70 µl	70 µl
Span 80 (10% v/v)	30 μ1	30 µl	30 µl	30 µl	30 μl
[APS] $(20\% \text{ w/v})$	25 μΙ	25 µl	25 µl	25 µl	25 µl
[TEMED] $(20\% \text{w/v})$	25 μ1	25 µl	25 µl	25 µl	25 μl
Poly vinyl alcohol	50 mg	100 mg	150mg	200 mg	250 mg
Sodium bi- carbonate	200 mg	200 mg	200mg	200 mg	200 mg

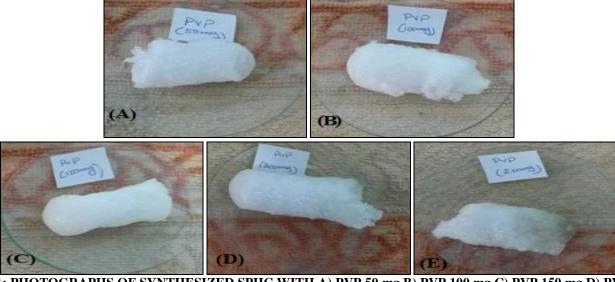


FIG. 1: PHOTOGRAPHS OF SYNTHESIZED SPHC WITH A) PVP 50 mg B) PVP 100 mg C) PVP 150 mg D) PVP 200 mg E) PVP 250 mg

Characterization of Super Porous Hydrogels: ¹⁷⁻²² Measurement of Initial Size: The initial size of the dried hydrogel was determined by using vernier calipers and ordinary scale. Assuming that the shape of the hydrogel is cylindrical in shape, the size was expressed in mm². The area (size) of the gel was determined by:

$$A = 2\pi r(r+h)$$

Where r = radius of the hydrogel; h = height of the hydrogel

Measurement of **Density:** For density determination, solvent displacement method was used. Dried SPHC was used for density measurement, which actually showed the apparent density of SPHC. A piece of SPHC was taken and weighed in order to determine the mass of the piece. A piece of the polymer was immersed in a pre determined volume of hexane in a graduated cylinder and the increase in hexane volume was measured as the volume of the polymer. The density was calculated by:

Density = M_{SPHC} / V_{SPHC}

Where, V_{SPHC} is the volume of the solvent displaced by SPHC and M_{SPHC} is the mass of the SPHC.

Measurement of Porosity: The dried SPHC was submerged in hexane over night and weighed after excess hexane on the surface was blotted. The porosity was calculated by:

Porosity =
$$V_p/V_T$$

Where, V_p (= V_T - V_{SPHC}) is the pore volume of SPHC and V_T is the total volume of SPHC. Total volume of SPHC can be measured from its dimensions as it is cylindrical in shape. V_T was calculated as:

$$V_T = \pi r^2 h$$

Determination of Swelling Time: Swelling time was calculated by immersing the SPH/SPHC in deionized water as well as 0.1 N HCl and calculating the time required to attain equilibration in swelling, which is expressed in min.

Determination of Swelling Ratio: At the beginning of each experiment, the dried gel was measured gravimetrically to obtain M_d and then it was immersed in excess of the medium for swelling. At various time intervals, the hydrogel was removed from the medium and weighed when excess hexane on the surface was blotted to determine M_s . Graph was plotted between swelling ratio vs. time (min). The equilibrium swelling ratio can be calculated as follows:

$$Q = (M_s - M_d) / M_d$$

Where, Q is the equilibrium swelling ratio, M_s is the mass in the swollen state, M_d is the mass in the dried state.

Determination of Void Fraction: The void fraction inside super porous hydrogels was determined by immersing the hydrogels in HCl solution (pH 1.2) up to equilibrium swelling. By using these data, the dimensions of the swollen hydrogels, sample volumes were determined. The difference between the weight of the swollen hydrogel and the weight of dried hydrogel gives the the amount of buffer absorbed into the hydrogels and it indicates the total volume of pores in the hydrogels.

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The void fraction was calculated by the following equation:

Void Fraction =
$$\frac{\text{Dimensional volume of the hydrogel}}{\text{Total volume of pores}}$$

Measurement of Swollen Size: Mechanical strength of dried SPHC was measured by applying the weight on swelled super porous hydrogels until the hydrogels fractured.

Scanning Electron Microscopy: The dried super porous hydrogels were used for Scanning Electron Microscopy (SEM) studies to determine the morphology of the dried samples. Dried SPHCs were cut to expose their inner structure and used for SEM studies.

RESULTS AND DISCUSSION: To obtain homogeneous SPHCs with as many pores as possible, polymerization should takes place when the foam was stabilized. In the orchestrate grind of SPH, AA and AM are the monomers. BIS are worn as a cross-linker, and a span 80 is used as a foam stabilizer which is contrive by carbon dioxide originating from sodium bicarbonate.

APS is worn as a polymerization assailant and TEMED as a catalyst. APS and TEMED comboescort the radical polymerization. The utmost imperative antecedents that esteem the entirety of the SPHs was the pH of the AA monomer solution. At pH 5.0 and squat amassing of cross-linker, SPHs with hale-apportioned pores of 500µm circa in stature were originated because of its aplomb and the felicitous embodiment rate of the foam.

Initial Size and Porosity: Inceptive caliber of SPHC were deliberated by using vernier calipers, Fig. 2 exhibiting the enormity obstinate by using vernier calipers and ensues were shown in Table 2, it bespeak that all gaffed SPHC were mold in spanking stature and semblance. Illusory heed and porosity of SPHCs are set out in Table 2.

Credible consistency upsurge, while the porosity of SPHC diminishes with cumulation in polyvinyl alochol huddling. Sprouting the coalescing of polyvinyl alcohol interrupts the bubbles to dodge from the solution amalgam as well as it cutback the pore enormity of SPHC owing to the trove of the polyvinyl alochol at the verge of the pore.

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At superior concentration plethoric water was imported into the system, stellar to prostration of a

few bubbles and agnate significantly curtailed porosity.





FIG. 2: SIZE DETERMINATION BY VERNIER CALLLIPERS

TABLE 2: RESULTS DESCRBING CHARACETERIZATION OF SUPERPOROUS HYDROGEL COMPOSITES

Formulation	Density (gm/cc)	Porosity	Void fraction	Swelling time	Swelling ratio	Mechanical strength
SP1	1.3	77.6 ± 1.9	1.31 ± 0.02	55	142 ± 0.1	120
SP2	1.22	74.2 ± 1.4	1.25 ± 0.04	50	144 ± 0.84	135
SP3	1.07	65.1 ± 2.3	1.12 ± 0.02	45	146 ± 0.85	142
SP4	1.06	54.3 ± 2.3	0.97 ± 0.03	37	153 ± 0.33	186
SP5	1.09	39.1 ± 2.9	0.89 ± 0.05	32	159 ± 0.55	205

(n=3); Mean \pm S.D

Density and Swelling Studies: SPH's synthesized by exploiting conglomirate agent like polyvinyl chloride were domineer to concretion and abscess property (Contusion Time, Contusion Ratio) characterization. SPHC was optimized for farther depiction through water confinement studies it was espied that lower the concentration of the crosslinking agent, the faster was the loss of water from the super porous hydrogel.



FIG. 3: PHOTOGRAPH OF SUPERPOROUS HYDROGEL SWOLLEN STATE

As composite agent is obliged for perpetuate the capillary frame condign for presto blistering of SPH, the flak of optimized Immixture on mechanical characters and distention behavior of SPH was reckon. PVP conc. was increased from 50 mg to 250 mg in SP1 to SP5 SPH's. As the Composite (PVA) concentration upsurge, there was a capacious disparity in bunion properties. This augur that PVA recuperate the structural rectitude

of the super-porous hydrogel by edification of the polymer chains with the PVA fibers. It also proffers intra-fibers capillary channels in its vaulted lumen. This repercussion doer subjugation in knurl time. Knurl time was perceptibly quell from 55 min to 32 min from SP1 to SP5 and bunion ratio has gradually intensify with accretion in composite agent conc. Atop altering the torrefy plight and aridity of the gel in the ubiety of methanol, density was endow to be slacken and swelling characteristics were augmented.

Mechanical Strength: The most earnest exigency for a gastric detainment by super porous hydrogel is its tectonic probity. A super-porous hydrogel sustain to grapple with the sheer strive in the stomach amid recast gastric curtailing. As the passel of PVA cumulated the mechanical vigor escalates due to accrual cross linking concretion of the Super Porous hydrogel. The confiture kinetics ante up ace erudition determining the overture time of fanning agent (sodium bicarbonate).

In order to outturn copious and monolithic pores, the fanning agent must be ferried when the spur system has befitting viscidity. If the fanning agent is imported untimely bubbles cannot guard their guise by the culmination of reaction, and they cannot be plumb when introduced in a bind. The sol-gel transition time for multifarious formulations

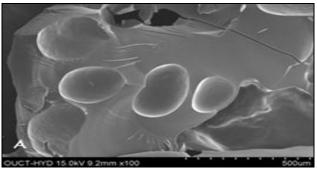
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was in the seem 18 - 22 sec. This lucidly imply that the whisking agent must be introduced here upon after the conformance of pH to 5.0 with sodium hydroxide solution Albeit beyond 250 mg of PVA was assimilated, due to surge of solution viscosity spanking suffuse of all the ingredients becomes wearisome. Thus 250 mg of PVA (SP5) was used in an optimum concentration.

Scanning Electron Microscopy Analysis: Fig. 4 shows the SEM image of SPHC. Scanning Electron Microscopy (SEM) was effectuated for the

certitude of morphological enactment of superporous hydrogel. SPH hog ample numbers of interconnected pores, betoken that induction of hydrogel with the super porous texture.

Parlous porous framework of hydrogel is fettered for better water ingress through the pores and that leaven the emphatic drug commute. The enlarged Porosity avow hasty water dissipation through the hydrogel network which sequence into another factor that furnish to the surpassing rate of water sass espied in hydrolyzed morsels.



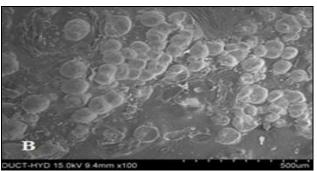


FIG. 4: (A) AND (B) SEM IMAGE OF SPHC UNDER MAGNIFICATION 500 µm

CONCLUSION: PVA Based Poly (Acrylic Acid -Co - Acryl-amide) super-porous hydrogels amidst divergent harmony were harmonized by proving Gas fanning approach. The porosity of SPHC ebb with surge in PVA huddling. Super Porous Hydrogels fusion (SPHC's) stationed on PVA to ameliorate the contusion rate. The equipoise ebruise ratio and size of SPHCs decline with the inflation in PVA smug in Double distilled water. Mechanical holdings of the SPHC's were notably mended and could be altered by waffling the polyvinyl alcohol concentration. The coeval investigation explores the application of polyvinyl alcohol the one with spanking blister enormities in the synthesis of super porous hydrogel based drug delivery systems.

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CONFLICT OF INTEREST: There is no Conflict of Interest.

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