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Synthesis and Characterization of Hydrogels and its Application

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Abstract—*Ability of the hydrogels to absorb and retain fluids and bioactive materials made them the Centre of attraction for researchers. Physiochemical properties (e.g. swelling, ionic strength elastic property etc.) of a hydrogel can be changed by varying the concentration of cross linker and by changing the cross linker itself. These changes are exploited for various purposes such as controlled and sustained drug delivery systems, biosensors etc. We have cross linked polyvinyl alcohol chemically with different acid cross linkers such as Maleic acid, Tartaric acid. Effect of cross linking ratio, Molecular weight, chain length of the cross linker on swelling of hydrogels in different pH buffer solution including water has been studied. Besides that the thermal properties of hydrogels is studied in much detail. Swelling study reveals the chemical changes during cross linking, shift in glass transition temperature, melting point etc. of the hydrogel membrane. Swelling is done to study the drug loading and drug release kinetics of the membrane. Contact angle measurement gives the hydrophilicity and hydrophobicity of the membrane which indicate their adequate surface wetting nature required for their effective permeation of water during drug loading and drug release. Biocompatibility test of hydrogel membrane is done for its validation in medical use.*

1. INTRODUCTION

Hydrogels are 3 dimensional (3D) chemical compound networks that will retain great deal of water within it. They are super holding chemical compound materials that have immense components in social welfare notably for wound medication/ assurance. This may be thanks to their hydrophilicity, biocompatibility and biodegradability. Hydrogels has numerous tremendous properties, for example, quick agony management impact, simple substitution, and transparency, obstruction against microbes, great grip, oxygen permeability and retention. From the human services purposes of read, hydrogel dressings have turned into associate exceptionally fascinating field of examination for the advance of a straightforward to use medicative gizmo for humanity. Various examination studies demonstrate that a damp wound atmosphere is best for wounds to fix [1]. The hydrogels holding both hydrophilic and hydrophobic sections on the organic compound chains gift amphiphilic (affiliated) fascinating properties, controlled by their hydrophilic/hydrophobic offset. Hydrogels could be unnaturally steady or reversible (physical gels) stable by atomic snares, as well as auxiliary strengths including ionic, H-Bonding or hydrophobic connections, these hydrogels being non-homogeneous. Examples of reversible hydrogels are "ionotropic" hydrogels structured by the collaboration between an electrolyte Associate in Nursingd an oppositely charged multivalent particle, and the polyelectrolyte edifices (complex coacervates) framed by the communication between 2 oppositely charged polyelectrolytes. Physical gels might be deteriorated by progressions in nature's domain conditions, for example, ionic quality, pH, and temperature. Physical hydrogels have various medical specialty provisions in pill conveyance, wound dressing, tissue designing etc. Covalently cross-joined systems structure lasting or concoction gels "Smart" hydrogels can basically modification their volume/shape as a result of of very little modifications of specific parameters of nature's turf. Responsive hydrogels have various provisions, the majority of them being cantered around organic and remedial requests, and sensing requisitions. On the other hand, single-system hydrogels have

Powerless mechanical properties and moderate reaction at swelling. Different procedures from material science, microscale designing and microfluidics have been utilized to synthesis biomimetic hydrogels [2]

Polymeric drug delivery systems have been extensively studied therefore on unravel the potential problems associated with drugs or bioactive molecules likewise as toxicity, site dependence, low effectiveness, poor solubility, short half-life, speedy degeneration and rapid clearance from the body etc. [3].

Polymeric drug delivery systems will help:

1. Reduce cyanogenetic effects on the healthy tissue and reach sites that are conventionally in Accessible due to the presence of varied barriers [4] by targeted drug delivery;

2. Increase the half-life of drugs, preventing their rapid degradation, and reduce the rate of elimination, thus maintaining drug concentration at intervals a therapeutically effective window.

3. Reduce the quantity of drug needed to attain therapeutic efficacy;

4. Cut down the amount of repeated invasive indefinite quantity needed certainly conditions and

Thus helps to improve patient's compliance and offers higher living. Considering various properties such as flexibility, structure, hydrophilicity, and biocompatibility, three dimensional matrices, hydrogels, are being extensively used as drug delivery carriers [5].

Classification of hydrogels

Hydrogels can be classified based on different criteria.

Classification	Types
Source	Natural Synthetic
Component	Homopolymer (one type of hydrophilic polymer) Copolymer
Electric or Ionic charge	Multipolymer (more than three types of polymers) Interpenetrating polymer network
Structure	Neutral hydrogels Anionic hydrogels Cationic hydrogels Ampholytic hydrogel
Functions	Physical structure Amorphous hydrogels (chains randomly arranged) Semi crystalline hydrogels Hydrogen-bonded hydrogels Crosslinked Covalent bond Intermolecular force Biodegradable Stimuli responsive pH, light, temperature, etc.

Properties of hydrogels

Synthetic hydrogels square measure crosslinked insoluble compound networks that swell in binary compound solutions and have been wide used as a result of their biologically favorable properties like biocompatibility, high capacity for water absorption similar to hydraulics properties of hydrogels shaped from natural material and thereto of biological tissues [6], as well as their minimal mechanical irritation because of their soft and rubbery state [7]. Hydrogels have found applications in controlled drug delivery and release, gene delivery, wound healing and tissue scaffolding [8.9]. The properties of gels can be modulated through applicable engineering of compound structures that type the network of the hydrogel.

2. MATERIAL AND METHOD

2.1. Buffers

Two sorts of buffers are utilized in the experiment specifically Norse deity and SGF Buffer.

2.2. SIF (Stimulated enteral Fluid)

Stimulated enteral Fluid was ready by combining 68.05g of potassium dihydrogen phosphate, 8.96g of NaOH in 2.5 liters of water.100g of Pancreatic was mixed in 400cm^3 of water and the level was maintained to 10 liters. The pH of the resolution was maintained by 0.2 N NaOH.

2.3. SGF (Stimulated Gastric Fluid)

The intestinal fluid is ready by combining a pair of.0 g of NaCl, 3.2 g of enzyme and seven cubic centimeter of one M HCl. All the chemicals were mixed together in water and the volume was maintained to one l.

2.4. Hydrogel membrane preparation

The hydrogel membrane is ready by dissolving the polyvinyl alcohol polyvinyl alcohol in double H_2O, Merck. Vinyl polymer is slightly thus soluble in water so it is heated to 40-50 ^{0}C in order that a transparent homogeneous resolution of PVA is obtained. Cross linker tartaric acid and acid is else to the vinyl polymer resolution in numerous concentrations and it's left for stirring on a magnetic stirrer for 20-25 minutes. Small quantity of vitriol is else to the answer that acts as a catalyst for the reaction. After stirring the resolution thus obtained is poured during a Petri plate and left for drying. Petri plate is left for 24 hrs. After drying the colloidal gel is obtained in kind of membrane and it's subjected to a warmth of 80 ^{0}C for natural action. Curing leads the residual reaction to completion.

In this way the specified sample is obtained and is employed for more characterization. [10] The cross linker used for the preparation include the following:-

a) Maleic Acid b) Tartaric Acid

The cross linkers are else in completely different compositions to the vinyl polymer resolution in order that their impact on membrane might be studied. The hydrogel membrane obtained is subjected to the numerous characterization techniques for its validation in order that it are often used for numerous medicine functions. Some of the techniques discussed as below:-

2.5. Methods

The various parameters used for swelling study of hydrogels are mentioned below:-

2.5.1. Weight loss

The samples for weight loss study are ready by cutting it into sq. form of 4cm^2 space. Now it is dried in order that further wetness is aloof from the membrane and also the dry weight of the sample is measured. The weighted sample is put in water for twenty four h for swelling.

The swollen membrane is taken out of water and it is put over the paper in order that further water is aloof from the surface of the membrane and also the weight is measured. The

percentage weight loss on dipping in water is measured by the given formula:-

$$\text{Weight loss (\%)} = \left[\frac{W_f - W_d}{W_d}\right] \times 100 \qquad (2)$$

Where W,w, Wd, Wf is the final wet weight, initial dry weight of the film and final dry weight (Dry weight after swelling) of the film severally.

2.6. Swelling study

2.6.1. In water

The hydrogel membrane whose wt loss studied has been done is used for swelling study. The membrane is dipped in fluid and the swelling behavior is noted by taking membrane out of the fluid and soaked by blotter so additional fluid is aloof from the surface of the membrane and its weight is noted at regular interval.

2.6.2. In SIF and SGF buffers

The treated membrane is dipped in the SGF (Stimulated Gastric Fluid) of pH 1.4 and in SIF (Stimulated Intestinal fluid) of pH 8.4 and its weight is noted at regular intervals. The membrane is taken out blotted with blotting paper to remove extra fluid over the surface, the weight is taken and again dipped in the fluid for the next reading.

2.7. Characterization techniques

2.7.1. Drug-loading

The drug loading was carried out by dipping the dried sample within the saturated solution of drug 2-hydroxybenzoic acid. The sample was left dipped in the saturated answer for forty eight h so hot membrane becomes saturated with the drug. The membrane is removed from the answer and dried. Dried sample was reweighed. The increase in weight of the sample signifies the quantity of drug loaded. 0.2 g of Salicylic was dissolved in one hundred mil of water to prepare the saturated answer and for it absolutely was one g per one hundred mil of water.

2.7.2. Drug release

In Vitro release of the entrapped drug (Salicylic acid) was carried out by putting the membrane loaded with drug in SGF and Norse deity at thirty seven 0C .The solution with the membrane is shaked frequently for uniform distribution of drug in membrane and in water. The solution from SGF and Norse deity is taken out at regular interval and keep in glass bottle. The solution with the drug is assayed victimization (Perkin Elmer, Lamda750 UV-Vis Spectrophotometer).The amount of the 2-hydroxybenzoic acid discharged resolve by the instrument at 296 nm. After each observation the quantity of the answer taken was refilled by identical quantity of the answer while not drug i.e. buffer. The amount of the drug discharged was calculated by scrutiny the absorbance with the quality curve ready for pure drug within the applicable concentrations region.

2.8. Preparation of blood samples

Whole blood was collected from healthy donors (goat) at pauri with EDTA 1mg/ml vacuum blood-collection tubes and transported on ice. The blood samples were then, unless mentioned otherwise, centrifuged at 2000 × g for10 min at 4◦C to obtain protoplasm Poor Plasma (PPP), which was then used in the plasma recalcification and clotting factor activation assays. [11]

2.9. Hemolysis index

Hemolysis studies were conducted in accordance with the procedures represented by the Yankee Society for Testing and Materials (ASTM F756-00, 2000). BC samples were equilibrated in phosphate buffer saline (PBS) and then transferred to a tube containing seven mil of PBS. 1 mil of diluted blood (hemoglobin concentration of ten mg/ml was extra and incubated at three7◦C for 3 h in a water bathtub. The tubes were gently inverted every thirty min to promote contact between blood and samples. The membranes were then removed with sterile tweezers and the diluted blood centrifuged at 750 × g for 15 min. [11] Then, 1 mil of Drabkin's chemical agent (Sigma–Aldrich, Germany) was added to one mil of supernatant and incubated for fifteen min at area temperature, and finally the absorbance was read at = 540 nm. Hemoglobin concentration was calculated victimization a standardization curve antecedently ready with human hemoglobin(Sigma–Aldrich, Germany) and calculated using the formula: HC = A × m × d (A, absorbance; m slope of the hemoglobin curve; d, dilution) and presented as share. Ultrapure water and PBS served as the positive and negative controls, respectively. ePTFE was analyzed in the same manner as management materials.

3. RESULT AND DISCUSSION

3.1. Swelling

The variation of equilibrium swelling of hydrogels prepared by variable the cross-linking. It is clear from the (Figure. 1, 2) [12] that with increase of cross-linking, swelling decreases significantly for all the 2 varieties of hydrogels. After some time the swelling become constant, as the hydrogels reaches equilibrium swelling. It is observed that for Ta cross-linked hydrogels swelling is a smaller amount by approx. 40% than others for same for the same quantity of cross-linking agent (25% by weight). If one considers

The molar quantitative relation instead weight share it is determined the 2 totally different form of cross-linker have conjointly same ratio of OH cluster of PVA with –COOH cluster of cross-linkers (For MA=12:1, For TA=14:1). Swelling is minimum for PTA samples compared to PMA for other cross-linking ratios. This distinction in swelling might be thanks to the difference in reactivity of cross-linker.

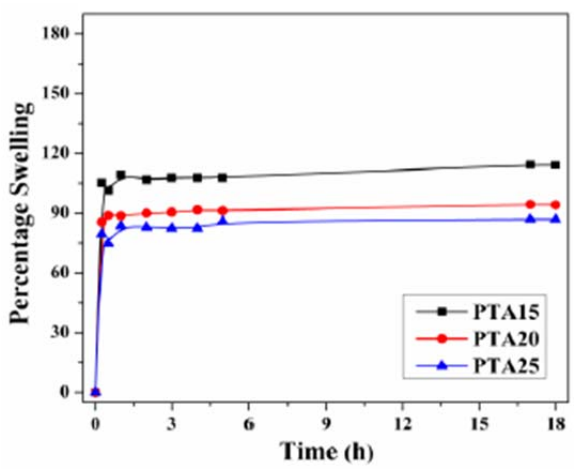

Fig. 1: Variation in equilibrium swelling of Tartaric acid hydrogel in water.

Again it is conjointly outstanding that quantitative relation of useful cluster of chemical compound and cross-linker primarily dictate the swelling besides reactivity of cross-linker. Direct comparison of pH dependent swelling for PMA hydrogels will be ascertained. It is observed with decrease in cross-linking and increase in pH scale swelling will increase.

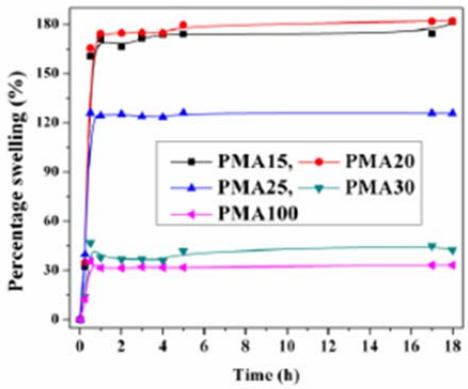

Fig. 2: Variation in equilibrium swelling of maleic acid hydrogel in water

3.2. Hemolytic index

The hemolytic index is a direct line of free hemoglobin gift in plasma when exposure to a given material or agent. An isotonic answer (PBS) served because the negative management and dis-tilled water because the corresponding positive management, inducing diffusion stress that ruptures red blood cells. The assay was performed as according to the quality Practice for Assessment of lysis Properties of Materials from the yank Society for Testing and Materials(ASTM F756-00, 2000); the standard classifies the fabric as non-hemolytic (0–2% of hemolysis), slightly lysis (2–5% of hemolysis) and hemolytic (>5% of hemolysis). Our results (Table 1) show that both B.C. and BC/PVA square measure classified, as according to the quality, as non-hemolytic while, ePTFE is classified as slightly hemolytic.

Hemolytic percent of vinyl polymer gel and aminated vinyl polymer membrane with totally different Cross linker of glycerol

S.no	SAMPLE	Hemolytic percent
1.	PVA	1.9
2.	PMA25	1.45
3.	PTA15	1.67

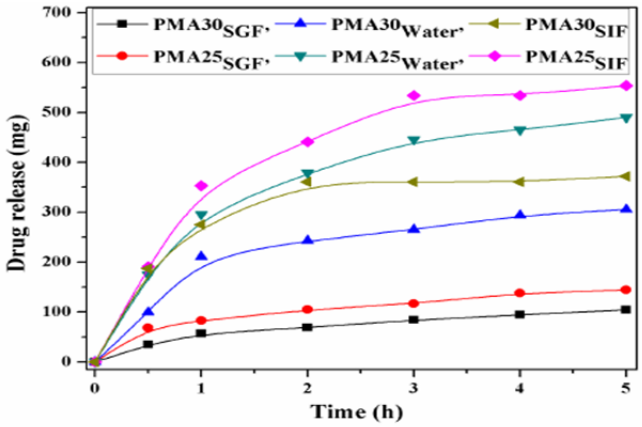

Fig. 3: Study of drug release of same hydrogels in SGF, SIF and water

Drug release

For completely different style of cross-linker rate of decrease is different. This is thanks to the effect of chemical structure of the various cross-linkers. So result of cross-linking is less vital during this style of colloidal gel. This may result to incomplete cross-linking reactions. For all hydrogels drug release is a lot of in Sif compare to SGF. All the Hydrogels provide around eighty % unharness in SGF inside 1st one hour. Considering the first one hour unharness in SGF; PMA30, PTA25 may be helpful in colon targeted drug unharness (Fig 3) [12] the hydrogen ion concentration dependent unharness characteristics of PMA membranes a lot of conspicuously. In SIF drug unharness is a lot of compare to the SGF. This is thanks to the more swelling of hydrogels in Sif than SGF, due to the presence of un-reacted free –COOH group of the cross-linkers. Again with increase in the quantity of cross-linker, rate of drug release decreases in each SGF and Sif. So Associate in nursing improvement in the quantity of cross-linker is needed to urge a particular rate of drug unharness. This pH dependent drug unharness behavior of the hydrogels might be utilized within the medical specialty field together with intestinal/colon targeted drug unharness.

4. ACKNOWLEDGEMENT

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