"BIODEGRADABLE HYDROGEL- ANALYZING THE IMPACT AND SENSITIVITY OF TEMPERATURE AND pH CHANGE"

Aayush Goel
Department of Polymer Science Chemical Technology
Delhi Technological University *(Formerly Delhi College of Engineering)*

Preparation of partially biodegradable hydrogel that changes its shape and volume in response to change in temperature and/or pH by UV irradiation of structure comprising dextran-maleic acid monoester and N-isopropylacrylamide.

Hydrogels are a class of materials, which contain large volumes of water in their swollen three-dimensional structure without dissolution. Because of the similarity between this highly hydrated three-dimensional network and hydrated body tissues as well as highly biocompatible property, the hydrated soft hydrogels have been widely used as biomaterials for drug control/release purpose. Generally, hydrogels are divided into two categories: conventional and intelligent; the latter can respond and change their shape and volume upon external stimuli, such as pH, temperature, photo field and antigen.

Recently, hydrogels, particularly the temperature sensitive ones, have pulled in broad enthusiasm because of their potential and promising applications in many fields, for example, protein-ligand acknowledgment, immobilization of chemical, on-off switches for adjusted medication conveyance or artificial organs. Among the family of temperature intelligent hydrogels, poly (Nisopropylacrylamide) (PNIPAAm) hydrogel is among the most widely studied. It shows a lower critical solution temperature (LCST) or transition temperature (Ttr) at B33C in aqueous solution and exhibits a sudden thermo reversible change in volume as external temperature cycles around this critical temperature. PNIPAAm hydrogels are usually formed by the covalent crosslinking of PNIPAAm chains with a commercial crosslinking agent like N,N0 -methylenebisacrylamide (MBAAm). PNIPAAm hydrogels are non-biodegradable, which may restrict their applications as biomaterials.

The biodegradability to a biomaterial is self-evident due to the absence of a chronic foreign-body reaction, which usually accompanies with the permanent presence of the non-biodegradable materials. Furthermore, the devices made from biodegradable materials do not require additional surgery to remove them. So, there is a need to create non-harmful, biodegradable hydrogels for the

biomedical applications without losing their shrewd properties, for example, temperature sensitivity. Many synthetic biodegradable hydrogels have been prepared from traditional biodegradable polymers, such as polylactide. But these polymers usually do not respond to the changes of the environmental stimuli. Recently, Jeonget al announced a biodegradable hydrogel framework having thermo-reaction ability, which comprised of blocks of polymers, for example, poly (ethylene oxide) (as non-biodegradable part) and poly (l-lactic acid) (as biodegradable segment). These hydrogels were produced from the reversible sol-to-gel transitions of the aqueous solutions of the copolymers.

Such sol-to-gel transitions were through the reversible physical crosslinking, such as coil-to-helix transition and hydrophobic association, etc. They suggested that there existed a critical gel concentration in the copolymer system, which was inversely related to the molecular weight of the polymers used. Around the critical gel concentration, sol–gel phase transition took place and thermosensitive property was achieved. In addition to the above reported reversible physical crosslinking approach for preparingthermosensitive biodegradable hydrogels, an approach based on chemical crosslinking for preparing biodegradable and thermosensitive hydrogels appears to be highly desirable. Kumashiro et al and Huh et al recently reported a temperature sensitive polysaccharide, based on the grafting of a temperature sensitive polymer (poly(NIPAAm-co-N,N-dimethylacrylamide) (co-polyNIPAAm–DMAAm) onto dextran antecedent followed by cross linking of the grafted cross linking of the grafted dextran forerunner with 1,6-hexamethylenediamine cross linker. They found that, at a temperature below LCST, the degree of enzymatic biodegradation of dextran hydrogel grafted with temperature-sensitive NIPAAm–DMAAm copolymer was decreased as the grafted copolymer length expanded; this graft-length dependent enzymatic biodegradation of grafted dextran, however, was not observed at a temperature above the LCST of the grafted segments.

TYPES

Gels are generally of two types

1. Organogel

2. Hydrogel

Organogel:

Organogel is defined as a thermoplastic, non-crystalline solid material composed of a liquid organic phase in a 3 dimensional crosslinked polymer networks.

Hydrogel:

They contain water soluble groups such as such as COOH, OH,CONH2,NH2, and SO3H.They have high capacity to absorb water it can be thousand time of weight of polymer. Because of its combined glassy and elastic behavior they have many applications and are highly studied. Hydrogels have been used in the fields of Biotechnology, Medicines, pharmacy, food industry, agriculture etc. Hydrogels are 3 dimensional cross linkedhydrophilic polymers that swell in water and watery arrangements without dissolving in them. Delicate quality, adroitness and ability to store water make hydrogels one of a kind material. Many strategies have been accounted for the synthesis of hydrogels like copolymerization/crosslinking of co-monomers utilizing multi functional co-monomer, which acts as a cross linking specialist. They can be classified in different courses based on their preparation method, polymer, biodegradable properties and sensitivity to encompassing condition and furthermore their application. Hydrogels being bio compatible materials have been perceived to work as medication defenders, particularly for peptide and proteins from invivo condition. Hydrogels that are receptive to particular particles, for example, glucose or antigens can be utilized as bio sensors and in addition sedate conveyance framework. Hydrogels can be set up from normal and engineered materials.

CLASSIFICATION BASED ON SOURCE

1. Natural
2. Synthetic

Classification according to polymeric composition

Depends on polymeric composition hydrogel classified in three types

(a) Homo-polymeric hydrogel are referred to polymer network formed from a single monomer, which is a basic unit forming a polymer network. Homo polymers have cross-linked structure depending on the polymerization technique and nature of the monomer.
(b) Co-polymeric hydrogels are referred as polymeric network of two or more different monomer species in which at list one is hydrophilic in nature. The monomers can arrange in a random, block and alternating form along the chain of the polymer network.
(c) Multi-polymer interpenetrating polymeric hydrogel (IPN)
A vital class of hydrogels is made of two autonomous cross-connected engineered and natural polymer components, contained in a network form. In semi-IPN hydrogels, one component is a non-cross-linked polymer and other component is a cross-linked polymer .

Depending on pore size they are classified as:

Type	Morphology	Major swelling mechanism	Swelling rate	Application
Non-porous	Without network porosity	Diffusion through free volumes	Very slow, sample size-dependent	Contact lenses, artificial muscles, Etc.
Micro-porous	Variation porosity with closed-cell structure (100-1000 A)	Combination of molecular diffusion and convection in the water filled pores	Slow, sample size-dependent	Mainly in biomedical applications and controlled release technology
Macro-porous	Various porosity with closed-cell structure (0.1- 1 μm)	Diffusion in the water filled pores	Fast, sample size-dependent	Mainly in form of superabsorbent in baby diapers, etc.
Super-porous	High porosity with interconnected open-cell structure	Capillary forces	Very fast, sample size-dependent	Drug delivery (particularly in the gastrointestinal tract), tissue engineering, etc.

Table: Types of hydrogel on the basis of pore size.

LITERATURE REVIEW

Hydrogels are solid jelly like materials that can have properties ranging from soft and brittle to hard and robust. It is a material that consists of a cross linked polymer network swollen by water and several studies have been conducted with a focus on this versatile material's properties. Choice of different monomer and cross linking agents can yield distinct hydrogels with unique properties for use in applications ranging from diapers to drug delivery. The possibility of tailoring the physicochemical properties of a hydrogel combined with its ease of preparation makes it a forerunner in many fields.

We have reviewed the incorporation of nanofillers in hydrogel networks and their ramifications on mechanical properties and morphology. The synergistic properties of the composite that are missing in the individual segments set up filled hydrogels as a cutting edge, adaptable class of materials with wide ranging potential applications. Nanoparticle-hydrogel composites have multifunctional

and jolts responsive properties that make them perfect for "smart" materials including optoelectronic switching devices, antimicrobial gels/matrices, soft material catalysts etc. The potential uses of these composites incorporate safe, clinically implantable nanoparticle-hydrogel composite frameworks for bio-detecting, recyclable reactant nanoparticle hydrogel composites for synthetic amalgamation and composite hydrogel patches for restorative applications. Control of the covalent interactions by engineered plan and forecast of the resultant filled hydrogel properties are rising as roads for explore. Such forecasts upon trial investigation would create the up and coming age of nanoparticle-hydrogel composites with ideal properties for a specific application. Later on, the improvement of these new age composites won't just make materials for cutting edge applications yet additionally control the comprehension of material associations, helping computational expectation to precisely figure the properties of the composite given the individual segments.

PROCEDURE

Materials and Methods:

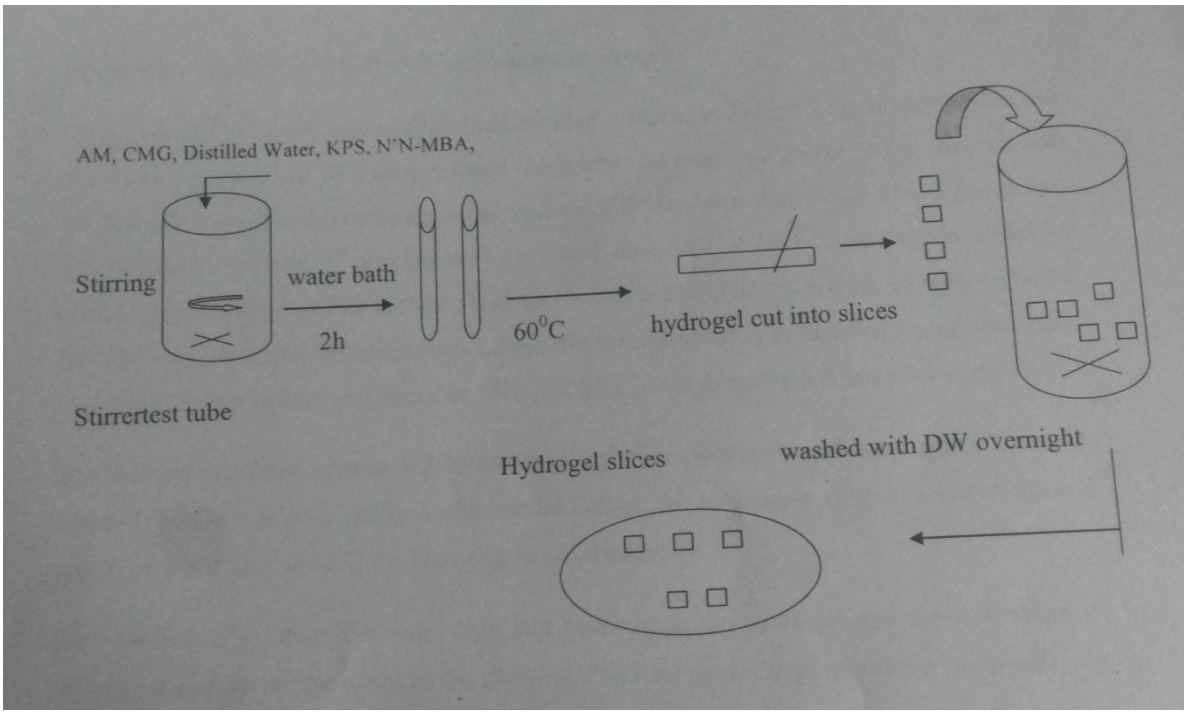
Dextran-maleic acid (10-75%), N-isopropylacrylamide (90-25%), Distilled water, 0.5N Ethanoic acid were used a received.

Synthesis of the Hydrogel:

Take 100ml beaker and add 25ml of distilled water in it. Weigh 2.0g of Dextran monoester and dissolved it in distilled water inside the beaker, put the beaker on magnetic stirrer. After that N-isopropylacrylamide is gradually added in a quantity of 0.11gms. The stirring was carried out for 15 minutes. Maleic anhydride (3.26gm) was added. The molar ratio of 1:1 is maintained between dextran and anhydride hydroxyl group.

The mixture is stirred fir approx. 1 hour or till it attains gel formation. The solution is poured into test tubes and keeps it in water bath at 60C.

Take out test tubes from the water bath and break open the hydrogel and cut into slices of 1cm and then transfer the slices in the distilled water for removal of unreacted chemicals, stir initially and intermittently for 2hr and keep it overnight. Next day change the distilled water and stir it for 1hr after that dry it in open atmosphere for 4-5 hours and then dry in vaccum oven at 60C till xerogel is formed.



FLOW DIAGRAM OF HYDROGEL PREPARATION

Swelling measurement:-

Swelling in distilled water

Dried hydrogel pieces were utilized to decide the level of swelling. The Swelling proportion (SR) was dictated by submerging the hydrogels sample in distilled water (50 ml) and was permitted to soak water at room temperature. After each 10min for 1hr then after each 30min for 4hr then after each 1hr up to saturation point is achieved, they were expelled from the water, smudged with filter paper to evacuate surface water and after that weight the hydrogel.

The swelling proportion (Sr) was computed utilizing the equation underneath:

$$Sr = \frac{(Wd - Wd) * 100}{Wd}$$

Where, Wd and Ws are the weights of the examples in dry state and swollen in water separately.

Effect of Temperature on swelling:

Dried hydrogel pieces were used to determine the degree of swelling. The Swelling ratio (S_R) was determined by immersing the hydrogels sample in distilled water at different temperature and was

allowed to soak. After every 10min for 1hr then after every 30min for 4hr then after every 1hr, they were removed from the water, blotted with filter paper to remove surface water and then weight the hydrogel.

The swelling ratio (S_r) was calculated using the equation below:

$$Sr = \frac{(Wd - Wd) * 100}{Wd}$$

Where, Wd and Ws are the weights of the samples in dry state and swollen in distilled water at different temperature solution respectively.

Effect of P_H on swelling:

First form the solution of different pH (2, 4, 6, 7, 10). Dried hydrogel pieces were used to determine the degree of swelling. The swelling ratio (S_R) was determined by immersing the hydrogels sample in different P_H solution and was allowed to soak solution at room temperature. After every 10min for 1hr then after every 30min for 4hr then after every 1hr, they were removed from the water, blotted with filter paper to remove surface water and then weight the hydrogel.

The swelling ratio (S_r) was calculated using the equation below:

$$Sr = \frac{(Wd - Wd) * 100}{Wd}$$

Where, Wd and Ws are the weights of the samples in dry state and swollen in different solution respectively.

RESULTS AND DISCUSSION

The samples were prepared by following the procedure as mentioned above. We have collected 3 samples and the results shown below are the experiments conducted on these samples. We have performed tensile tests, flexural tests, SEM tests, water retention capacity and pH swelling tests.

The readings obtained are given below:

MECHANICAL PROPERTIES

COMPARISON OF TENSILE TEST.

SAMPLES	Tensile extension at Maximum Load (mm)	Tensile stress at Maximum Load (MPa)	Extension at Break (Standard) (mm)	Modulus (Automatic) (MPa)
Sample 1	7.63726	-0.67134	8.21328	69.85503
Sample 2	5.64529	-0.25841	8.05031	373.5652
Sample 3	3.02136	0.53270	3.28344	229.45901

Sample 1 showed a tensile modulus of 69.8MPa while sample 2 showed a nearly 500% increase in modulus. However, sample 3 showed a reduction in modulus from sample 2 but was about 200% greater than that of the sample 1.

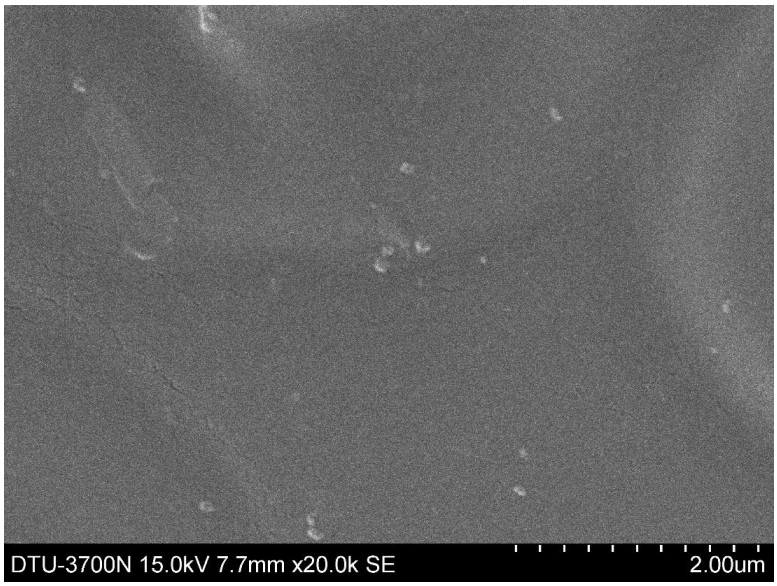
COMPARISON OF FLEXURAL TEST.

Samples	Maximum flexural load(kN)	Flexural stress at maximum flexural load(MPa)	Extension at maximum flexural load(mm)	Maximum flexural extension(mm)	Flexural strain at maximum flexural extension(%)
1	0.37186	557.85431	-3.65859	3.86281	3.00656
2	0.44304	272.00607	-1.48359	1.65203	1.73188
3	0.32072	206.60481	-1.94203	2.15937	2.22776

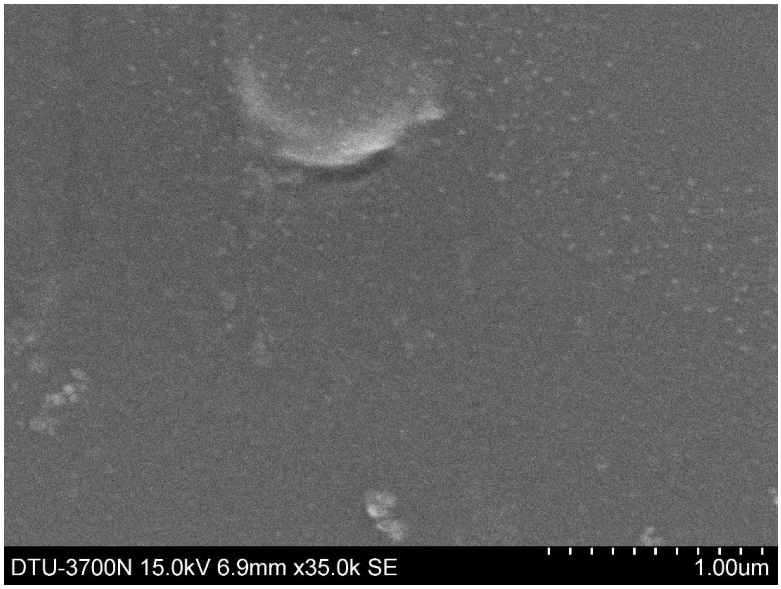
We infer from the table that the sample 1 exhibited maximum flexural stress at maximum flexural load followed by sample 2 and lowest in sample 3.

Hence, sample 1 was able to bend under the effect of given load to a least amount thus proving as a strong sample with better mechanical properties.

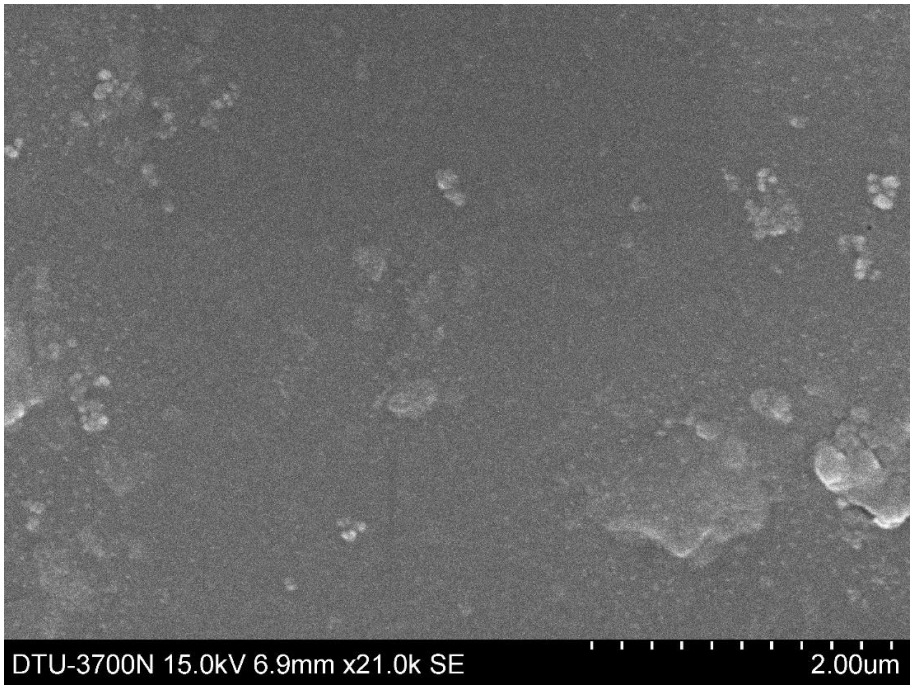
SEM image for sample 1



SEM image for sample 2



SEM for sample 3



Sample 1- Pure hydrogel formed by Dextran-maleic acid and N-isopropylacrylamide.

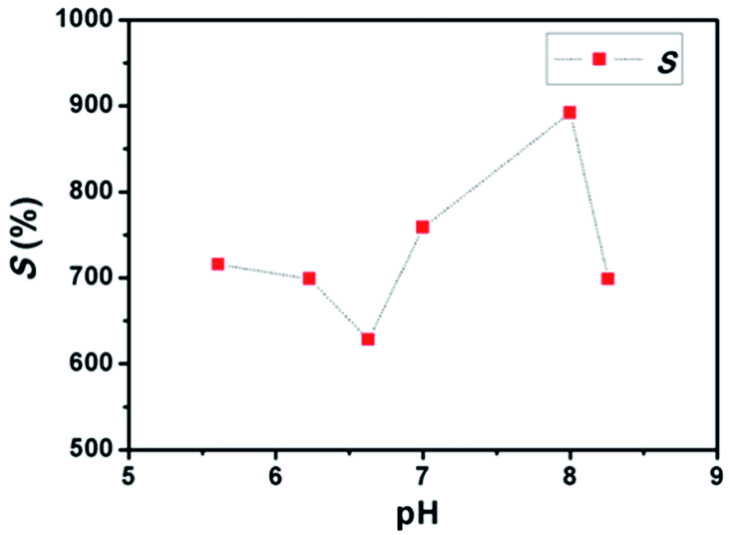
Sample 2- Hydrogel with 10% Dextran-maleic acid.

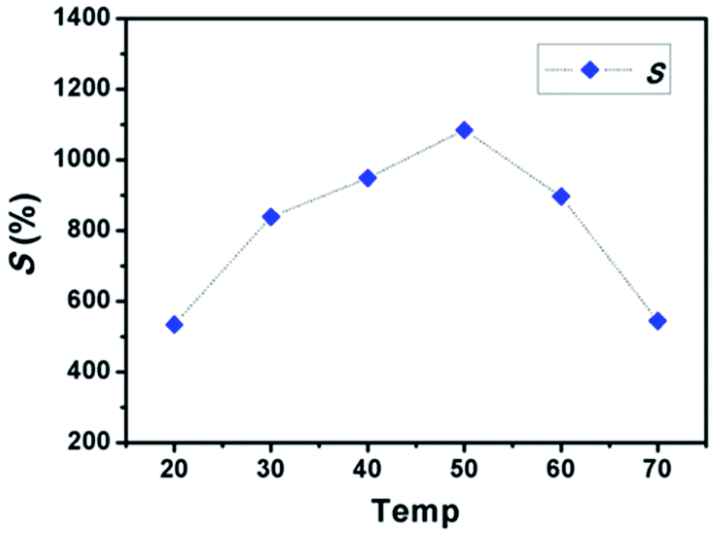
Sample 3- Hydrogel with 20% Dextran-maleic acid.

SWELLING EFFECT:

Out of the two samples we took all the three samples for an effective study and carried and calculated the swelling and effect of Ph and temperature change on the shape and volume of the samples. We made the calculations for each sample 2 times i.e first observation at time=0sec and the second one at time= after 30min on the same sample with varying pH and temperature.

The results obtained were as follows:





CONCLUSION

On the basis of experiments carried out we observed that for different concentration of samples the mechanical properties, the SEM test and the swelling property the results obtained were somewhat satisfactory.

The main focus was on how the hydrogel would react when it would be held under different temperature conditions and would be reacted under different pH range. We, from the graph observed that when the concentration of dextran maleic acid was increased the samples were showing mixed behaviour while the pure sample was behaving brilliantly and was showing effects as per the need.

While the study has not been completely done, thus from the research done we can just figure out that this type of hydrogel can be used in medical applications if some research can be carried out properly.

At the end, we will just be concluding with the fact that whatever samples were prepared by us showed great results and that, the properties of **DEXTRAN MALIEC-ISOPROPYLACRYLAMIDE HYDROGEL** can be widely used.