A Study on the Thermal Responsive Behavior of Hydrogel Based Materials and their Potential Use in Medical Applications

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ISLAMABAD, PAKISTAN.

DECEMBER, 2017

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A thesis submitted in partial fulfillment of the requirement for the degree of
MS Biomedical Engineering

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DECEMBER, 2017

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Acknowledgements

It is by the grace of Allah Almighty, the most merciful, that I have been able to accomplish this task, without His will and guidance, this work would not have been possible. I am profusely thankful to my beloved parents who raised me when I was not capable of walking and continued to support me throughout, in every department of my life.

I feel great pleasure in extending my heartfelt gratitude to my supervisor, Dr. Murtaza Najabat Ali, for his tireless efforts and continuous motivation. I would also like to thank Dr. Nabeel Anwar HoD BMES, Dr. Adeeb Shehzad and Dr. Shahrukh Abbas for being on my thesis guidance and evaluation committee.

I am extremely grateful to Miss Mariam Mir for her kind support, cooperation and help whenever I needed it. I am also thankful to Miss Bakhtawar Ghafoor and Miss Hafsa Inam for their guidance and positive criticism. I am greatly obliged to Mr. Muhammad Aamir for his assistance in the laboratory work.

My special thanks are due for my dearest friends Amna Zaigham, Amna Aleem Khawaja, Maliha Asad Khan, Kholood Janjua and Najwa Farooq for their timely advice and constant support.

I would like to mention the great help and support extended to me by my grandparents, my mother and father-in-law, and my sister-in-law. This work would not have been possible without their prayers and indispensable support.

I would also like to pay special thanks to my parents, Dr. Nabeela Akhter and Syed Mukarram Hussain, my brother Syed Talha Mukarram, and my husband Muhammad Junaid Farrukh for believing in me. There was no way I could do it without them around.

Finally, I would like to express my gratitude to all the individuals who have rendered valuable assistance to my study.

Dedicated to my loving grandparents, exceptional parents, dearest brother and supportive husband who have all been a source of constant motivation and kind prayers.

Abstract

Hydrophilic gels called hydrogels are cross-linked materials that absorb large quantities of water without dissolving. Their tendency to absorb water is due to the presence of hydrophilic functional groups attached to the polymer backbone and their resistance to dissolution is justified by the presence of cross-links between network chains. Responsive polymers can exhibit reversible or irreversible changes in their chemical structures and/or physical properties to an external stimulus such as pH, temperature, ionic strength, light irradiation, mechanical forces, electric and magnetic fields etc. Existing temperature sensing devices are infeasible for usage in internal body orifices and its difficult for them to be integrated with an implant because of poor flexibility characteristics, inappropriate size, configuration and geometry. The proposed thermal responsive hydrogel based sensor offers the potential to address these issues by synthesizing and investigating the thermal responsive properties of Chitosan-PEG hydrogels. This study proves its basic sensing capability, characterizes it fully, helps understand its behavior and defines its sensing span.

Keywords: *Hydrogels, thermoresponsive, medical applications*

Table of Contents

List of Acronyms

Polyethylene Glycol	PEG
Chitosan	Cts
Poly(vinyl alcohol)	PVA
Sodium Chloride	NaCl
Sodium Hydrogen Carbonate	$NaHCO_3$
Potassium Chloride	KCl
Pseudoextracellular fluid	PECF
Revolutions per minute	rpm
Room Temperature and Pressure	rtp
Dry Weight	W_{dry}
Wet Weight	W_{wet}
Swelling Ratio	SR
Fourier Transform Infrared Spectroscopy	FTIR
Potassium Bromide	KBr
X-Ray Diffraction Analysis	XRD
Scanning Electron Microscopic	SEM
Kilo Volt	kV
Silver/Silver Chloride	Ag/AgCl
Personal Computer	PC
3 dimensional	3D
Data Acquisition	DAQ
Analog-to-Digital Converter	ADC

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CHAPTER 1 INTRODUCTION

Stimuli-responsive polymers uniquely undergo a reversible phase transition in response to exposure to external stimuli, including temperature, pH, mechanical forces, light, electric and magnetic fields. This feature has attracted much interest for their usage in the field of medicine and biotechnology, for example in drug delivery systems.

Hydrophilic networks, that can absorb large amounts of biological fluids while being able to maintain a unique three-dimensional structure, are known as hydrogels. Their water absorbing property is due to the availabilty of hydrophilic groups. These groups are attached to the polymer backbone. On the other hand, the resistance against dissolving is justified by the presence of cross-links between network chains. Being high in water content, hydrogels have soft and rubber-like texture. This property gives hydrogels very close resemblance to soft tissues found in living organisms. For this reason, they can be designed to mimic the role of natural gels in living things, for example, swelling. But on the other hand, they differentiate from the natural gels too because they do not dissolve in water. They have the ability to entrap significant amounts of fluid and solutes, and take shape of a gel-like structure. Moreover, hydrogels are extremely biocompatible thus causing very little friction or irritation to the cells or tissues in contact with it. This makes them ideal to be used in artificial tissues and organ implants.

Currently, the hydrogels are being exploited for advanced functions, like drug carriers, gene carriers, both with controlled release properties, environmentally adaptive coatings, self-healing materials, catalysis, and in detection and imaging. Hydrogels are such polymeric materials that show major advantages over other alternatives, such as adjustable detection sensitivity, mechanical stability, convenient integration into detection device and biocompatibility.

This study particularly focuses on synthesizing and investigating the thermal responsive properties of hydrogel comprising of Chitosan and Polyethyelene Glycol (PEG). It also includes the characterization of this novel, thermally responsive hydrogel. Chitosan is a natural polysaccharide, having structural characteristics similar to glycosaminoglycans. Chitosan based hydrogels have lately been in focus for medical and pharmaceutical applications mainly because of chitosan’s favorable properties that include being biocompatible, bioabsorbable, mucoadhesive, non-allergenic, non-toxic, and easily available. It is known to aid in the process

of cell proliferation and has also been explored for the microencapsulation of several drugs. These properties make chitosan an outstanding candidate for biomedical applications, notably for dental and bone implants, cartilage, and artificial skin.

The other constituent of the proposed hydrogel is polyethylene glycol (PEG). It is a water soluble polymer that exhibits properties such as biocompatibility, hydrophilicity, protein resistance, low toxicity, and immunogenicity. Like chitosan, PEG is also used in many biomedical applications. It has been observed that PEG can revoke the immunogenicity of proteins and is capable of preserving their biological characteristics. Moreover, PEGs are used for improving the biocompatibility of polymers.

The combination of Chitosan and PEG is believed to have thermoresponsive characteristics. Thermoresponsive hydrogels undergo volume phase transition between swollen and shrunken states when exposed to different temperatures and physiological conditions. Since they swell or shrink depending on the environmental conditions, they can be designed for stimuli responsive drug delivery or controlled release systems. Temperature dependent volume change presents either Shrunken-swollen behavior, called thermoswelling or Swollen-shrunken behavior, referred to as thermoshrinking. The thermoresponsive behavior of hydrogels has attracted great attention due to fundamental and technological interests.

Biosensors detecting and converting biological reactions into a computable signal have been in much focus recently. Hydrogel, being a biocompatible polymer with great capacity for water absorption, can be used as a ground material in the formation of a hydrogel based biosensor. A typical biosensor system begins with the base materials having the sensing ability, and proceeds with the development and implementation of the desired strategies for sensing. The ground materials include metals, glass, polymers, or composites. Sensing strategies may be electrochemical, mass based, optical, etc. depending on the materials being used. One or more of these sensing strategies can be used for identification of a particular biomolecule using different methods such as conductometric, potentiometric, gravimetric, absorbance, and luminescence. Biosensors produce a computable signal originated by chemical reactions when an active biomolecule is integrated with a suitable transducer.

The main motivation behind this study was that the existing temperature sensing devices are infeasible for usage in internal body orifices. It is hard for them to be integrated with an implant because of their poor flexibility characteristics, inappropriate size and configuration,

impractical geometry. For example, drug eluting stents require temperature sensing ability, and a thermometer cannot be implanted in a stent or coronary artery implant. So, the proposed thermal responsive hydrogel based sensor offers the potential to address these issues. This study proves its basic sensing capability, characterizes it fully, helps understand its behavior and defines its sensing span.

CHAPTER 2 REVIEW OF LITERATURE

2.1 Introduction to Hydrogels

Hydrogels are crosslinked three dimensional networks of hydrophilic polymer chains that have the ability to store large amounts of fluid backed by their hydrophilicity. This results in the hydrogel networks having the ability to extensively swell in fluids. Since human body constitutes primarily of fluids and mainly water, a hydrogel is considered to have a great potential as far as biomedical applications are concerned. Recently, a lot of work has been going on to check the utility of hydrogels in different fields including their usage as biosensors, in drug delivery, tissue engineering, as self-healing materials, and hemostasis bandages. [1, 2]

In comparison to other biomaterials, hydrogels have characteristics such as greater biocompatibility, tunable biodegradability, viscoelasticity, porosity, ease of fabrication, etc. [3] But, on the other hand, their fragile nature makes them less feasible for a few applications. Therefore, hydrogels having greater strength and better stability characteristics are still to be researched on in order to exploit their potential fully.

Hydrogels may be composed of natural polymer chains like collagen or alginate or from synthetic polymers such as poly(vinyl alcohol) (PVA) and poly(ethylene glycol) (PEG). They could be made to mimic the features of natural gels found in living organisms such as swelling, but they differ from them in a way that they do not dissolve in water. Hydrogels are soft and rubbery in consistency and have the ability to store relatively high water content. These characteristics give them a strong resemblance to many soft tissues found in the living organisms. In addition to being highly biocompatible, hydrogels give minimal mechanical friction to the surrounding cells and tissues. Both of these features make them ideal to be used as artificial tissues and organ implants. Hydrogels undergo significant change in volume and/or mass because change in their fluid content. Even then, the state of water in the hydrated polymeric networks is more significant because it controls the interaction between the polymer and other substances, which is of great importance when the hydrogel is used as a bioactive carrier. [4] Furthermore, the state of water in the hydrogel can also affect its biocompatibility when it is used as an implant material. Lastly, in case of the hydrogel being used as an encapsulation material for enzyme, the state of water is believed to determine its reactivity and bioavailability.

2.2 Hydrogel Composition

The synthetically formed hydrogels are now replacing those formed naturally. This can help achieve improved durability, high water absorption capacity as well as improved mechanical strength characteristics. [5] Moreover, synthetic hydrogels with desired network structures, and adjustable mechanical strength can be developed by opting for different developing strategies. They can be prepared with artificial components and have great stability even when exposed to extreme conditions like high temperature or a very acidic or basic medium. [6] In addition to this, stimuli-responsive functional groups can be added to the polymer chains, thus resulting in the hydrogel having the property of changing in response to external stimuli including heat, pH, light, chemical agents, electric and magnetic fields. Although the hydrogels were first discovered in 1968 and they have been proven to provide a promising platform with huge potential for biomedical use since then, their applications in this field are still in a developing phase.

The composition of the proposed hydrogel is based on Chitosan and Poly(ethylene glycol). Chitosan is a polycationic copolymer of β-[1→4]-linked 2-acetamido-2-deoxy-$_D$-glucopyranose and 2-amino-2-deoxy-$_D$-glucopyranose. [7] It is generally obtained by alkaline deacetylation of chitin, which is the primary element of the exoskeleton of crustaceans, like shrimps. This makes the sources of chitosan to be abundantly found in nature, thus resulting in low cost of its production and easier availability. [8] Chitosan is believed to have a great potential to be used in biomedical and pharmaceutical applications, the reasons for which mainly include its biocompatibility, non-toxicity and biodegradability. This creates scope for it to be used in implants [9], or for topical ocular application [10] or injection [11]. In addition to this, chitosan can be considered as biodegradable because it is metabolized by certain human enzymes, such as lysozyme. It also promotes wound-healing [12, 13] and has bacteriostatic effects. [14, 15]

Poly(ethylene glycol) (PEG) also has favorable biological, chemical and physical properties like being hydrophilic, less toxic, and biocompatible. [16] Several studies have been published on hydrogels containing chitosan and PEG. [17] It has also been identified from viscometric studies that blends based on chitosan and PEG are compatible because of existence of attractive intermolecular interactions between their polymer chains. [18]

In most of the studies on chitosan-based hydrogels, glutaraldehyde has been made use of as the crosslinker. In the present study too, glutaraldehyde crosslinked hydrogel composed of chitosan and PEG is made and its swelling behavior is studied under different conditions.

2.3 Thermally Responsive Hydrogels

Hydrogels have now been known to be useful as smart materials because of their ability to produce intense volume change in response to a range of physical and/or chemical stimuli. The physical stimuli include temperature, light, pressure, sound electric or magnetic field, whereas chemical stimuli may be pH, ionic strength, molecular species and solvent composition, as illustrated in Figure 2.1. [19]

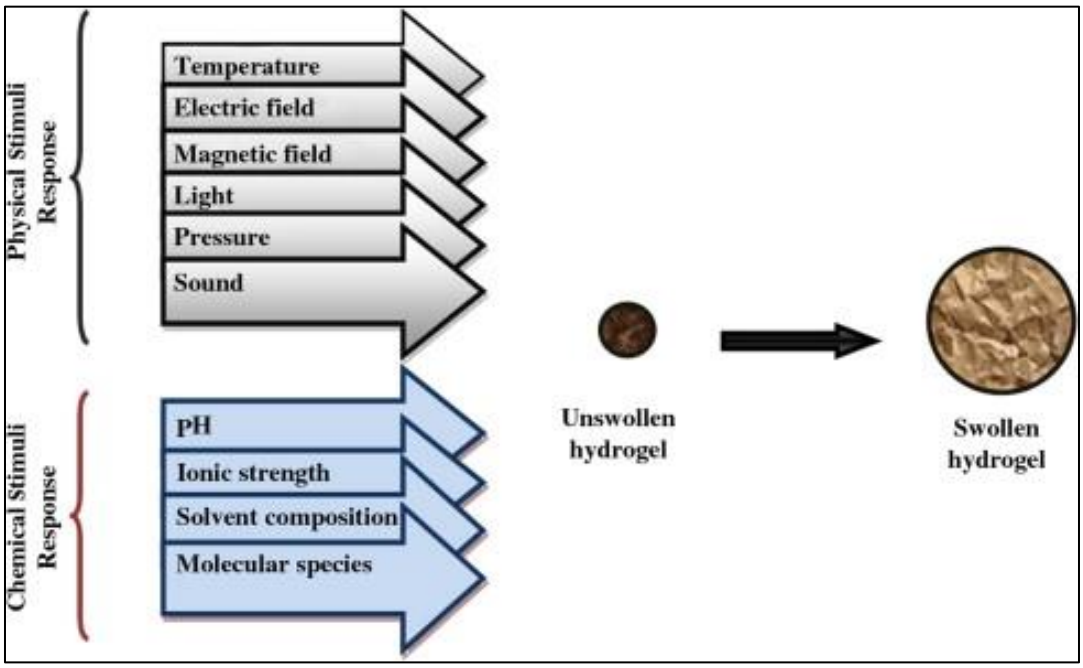


Figure 2.1: Stimuli response swelling hydrogel

Thermally responsive hydrogels modulate their volume phase transition behavior upon temperature change. In biomedical applications, exposure to temperatures varying between ambient temperature and physiological temperature can be employed. Their potential as in situ forming biomaterials has rendered these hydrogels very attractive. [20] The main component contributing to controlling the properties of a synthetic thermoresponsive hydrogel is the equilibrium between the hydrophobic and hydrophilic interactions. The exposure temperature greatly affects the hydrophobic interactions between hydrophobic polymer segments and the

hydrophilic interactions between hydrophilic polymer segments and water molecules. This then allows a small temperature change being able to interrupt the original equilibrium and thus induce volume phase transition. An example of this is the introduction of a hydrophobic segment such as ethyl or propyl to a hydrophilic polymer. This, as a result, adjusts the hydrophobicity of the polymer. Moreover, a small change in temperature causes negative change in the Gibbs free energy. This results in the elimination of polymer-water interaction and a more favorable water–water and polymer–polymer interaction. To balance out this negative Gibbs free energy, there has to be an increase in the entropy term due to the already known increased enthalpy term. Due to the dramatic increase in the hydrophobic interactions between polymer chains, the polymer chains quickly dehydrate and collapse to a more hydrophobic structure. [21, 22]

CHAPTER 3 MATERIALS AND METHODS

3.1. Materials

Polyethylene Glycol (PEG) with molecular weight 6000 g/m was obtained from Sigma-Aldrich. Chitosan (CS)-assay 90% was purchased from Avonchem (UK). Glutaraldehyde (Daejung Chemical Co.) was used as the chemical crosslinking reagent and was purchased as a 25% (wt. %) aqueous solution. Acetic Acid 100% (glacial) was purchased from Sigma-Aldric. All chemicals were used as such without further purification. Deionised water was used at different stages of the experiment.

Pseudoextracellular fluid (PECF) was used as the solvent throughout the course of experiment. Sodium Chloride (NaCl), Sodium Hydrogen Carbonate ($NaHCO_3$), Sodium Phosphate Monobasic Dihydrate was all purchased from Sigma-Aldrich while Potassium Chloride (KCl) was purchased from AppliChem Panreac.

3.2. Hydrogel Synthesis

Various compositions of the Chitosan-PEG hydrogel were synthesized to be tested thermo-gravimetrically. Hydrogels are mechanically friable especially when they have absorbed water. Cracks can form readily. We selected such compositions that maintained structural integrity when exposed to a hydrated environment for a long while, throughout the course of experiment. The compositions that were not mechanically stable enough, i.e. those in which crack formation began in the middle of experiment were declared unsuitable for this sort of sensing application and were discarded. After optimization of the hydrogel based on mechanical stability, 5 compositions were shortlisted as shown in Table 3-1.

Table 3-1: Shortlisted hydrogel compositions

Serial #	Chitosan (wt/vol %)	PEG (wt/vol %)	Chitosan-PEG Ratio
1	**3.33**	**2.33**	**6 : 4**
2	**3.33**	**4.33**	**4.35 : 5.65**
3	**3.33**	**3.33**	**1 : 1**
4	**2.33**	**3.33**	**4 : 6**
5	**4.33**	**3.33**	**5.65 : 4.35**

3.3. Synthesis Protocol

1% Acetic Acid solution was prepared by adding 1.2ml Acetic Acid to 120ml of deionised water. Chitosan (quantity according to the compositions in Table 3-1) added to this solution. The resulting solution is stirred at 40°C until complete dissolution of Chitosan is achieved. PEG (quantity according to the compositions in Table 3-1) was then added to this Chitosan solution. The solution is stirred at room temperature until PEG dissolves. Next, 200 μl of Glutaraldehyde is added as a cross linker while stirring at an rpm of about 1000. The solution is kept under continuous stirring continuously for approximately another 20 minutes and then poured into polystyrene Petri dishes. The synthesized hydrogel is left for oven drying (set at 37°C) for upto 12 hours.

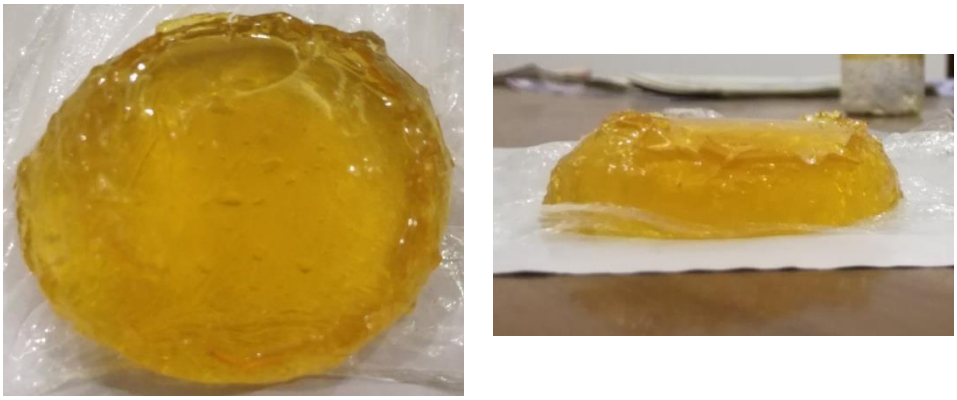


Figure 3.1: Semi-cured Chitosan-PEG Hydrogel

Pseudoextracellular fluid was used as the solvent throughout the experimentation, because it closely mimics the composition of the extracellular fluid present in the human body. To prepare it, Sodium, Potassium, Chloride, Bicarbonate and Biphosphate ions were added together in different ratios and mixed until they formed a transparent solution.

Table 3-2: Composition of PECF

Ion	Concentration(meq/L)
Na^+	145
K^+	5
Cl^-	118
$HC0_3^-$	30
$HP0_4^{-2}$	2

3.4. Hydrogel Thermo-gravimetric Testing (Volume Phase Transition behavior)

The selected hydrogel compositions that were observed not to crack readily and that showed the desired mechanical stability characteristics were each tested thermo-gravimetrically. The swelling behavior of the hydrogels was measured once immersed in PECF solution at different temperatures.

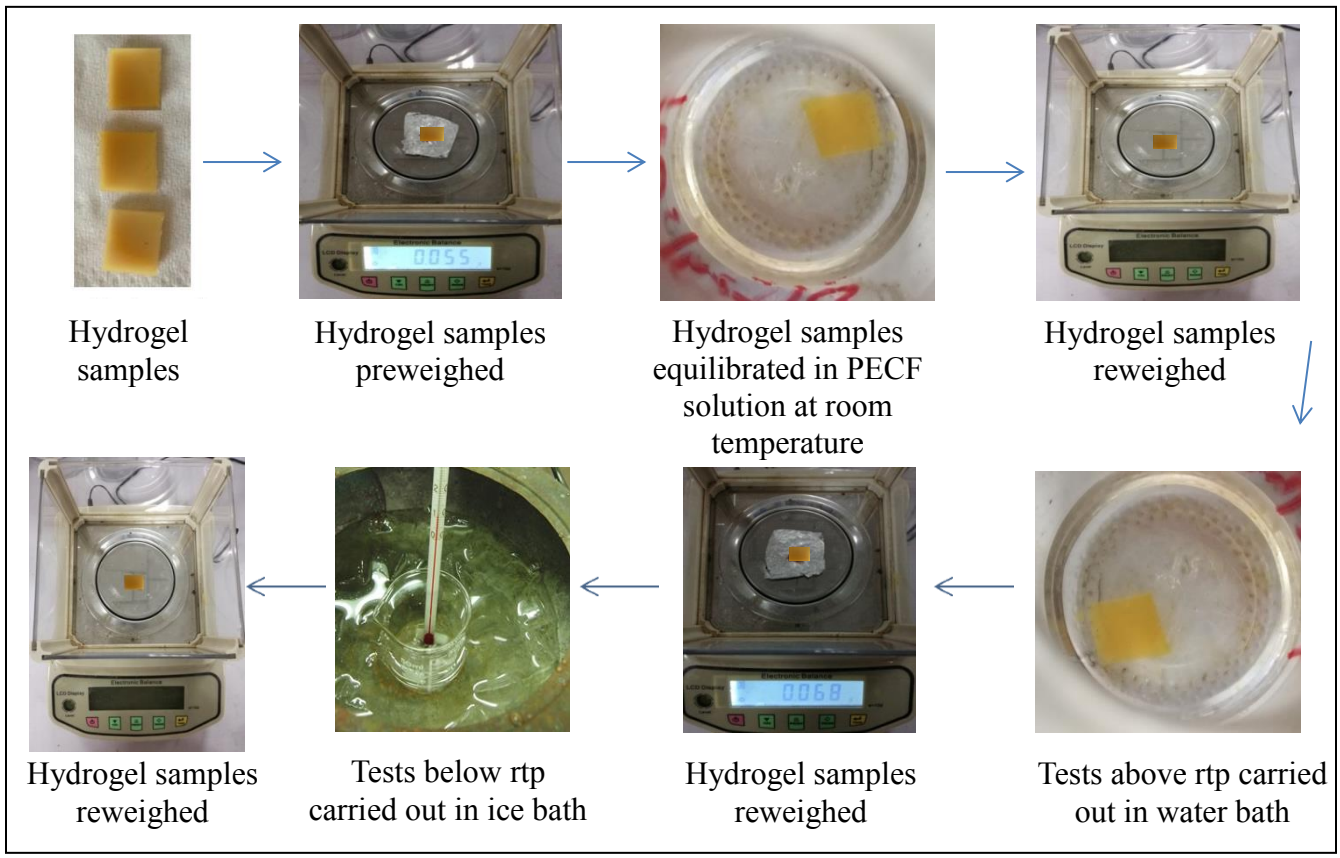


Figure 3.2: Experiment Protocol for Hydrogel Thermo-gravimetric Testing

Each hydrogel sample was preweighed (W_{dry}) on an electronic balance and then placed in a beaker containing 20ml PECF solution. The hydrogel was kept in this solution at room temperature until its weight attained a stable value. This was continued till no addition in weight was observed for at least five measurements. Each hydrogel sample had to be treated this way before further experimentation. Constant weight is an indication that the gel has reached equilibrium swelling state. Once equilibrium swelling state was achieved, the beaker containing

the same PECF solution that the hydrogel was previously exposed to was immersed in a water bath maintained at a particular temperature. The immersed hydrogel sample was then withdrawn from the solution after being exposed to the PECF solution at a particular temperature, for a set time period. The wet weight (W_{wet}) of the sample was determined after gently wiping its surface water with a filter paper and then weighing it immediately. Experiments were conducted in triplicates. The swelling ratio (SR) was calculated from the following equation:

$$\textbf{\textit{Swelling Ratio}}\ (g/g) = \frac{\textbf{\textit{Wwet}} - \textbf{\textit{Wdry}}}{\textbf{\textit{Wdry}}}$$

3.5. Characterization of Hydrogels

The selected hydrogel compositions that showed the desired mechanical stability characteristics and that showed good results as far as the thermo-gravimetric testing is concerned were further shortlisted for characterization. They were characterized by Chemical Structural Analysis, Crystallographic Analysis and Surface Morphological Analysis.

3.5.1 Chemical Structure Analysis

The Fourier Transform Infrared Spectroscopy (FTIR) was performed to identify the chemical bonds present in the samples by producing an infrared absorption spectrum. It helped perform the chemical characterization of the functional groups present and the types of interactions in the hydrogel samples. FTIR spectra were obtained in KBr mode, with wavenumber range from 4000 to 450 cm-s during 256 scans, with 8 cm^{-1} resolution (Perkin Elmer, spectrum 100 FTIR spectrophotometer).

3.5.2 Crystallographic Analysis

X-Ray Diffraction Analysis (XRD) is a rapid analytical technique that is used for the phase identification of a crystalline material, in this case, the hydrogel. It can provide information on unit cell dimensions of the crystalline material structure. The amorphous or crystalline structure of composite hydrogel was identified by X-ray diffraction (XRD) analysis. The diffraction pattern was obtained using a STOE X-ray Diffractometer, with Cu-K α radiation source (λ= 0.15418). The data was composed at 2θ between 10-70 degrees.

3.5.3 Surface Morphological Analysis

Scanning Electron Microscopic (SEM) provides detailed high resolution images of the sample by rastering a focused electron beam across the surface and detecting secondary or backscattered electron signal. SEM was performed in order to assess the surface morphology of the hydrogel samples. The equipment used was by using JSM-6490A Analytical scanning electron microscope (JEOL, Tokyo, Japan). The SEM images were acquired at an activation voltage of 5 kV.

3.6. Hydrogel based Temperature Sensor Testing

3.6.1 Sensor Fabrication

The sensor was composed of 2 silver wires, each of which was embedded into semi-cured hydrogel from one side as shown in Figure 3.3. The complete curing of the hydrogel resulted in shrinkage, thus leading to the hydrogel wrapping itself around the electrode. It was carefully noted that the total length of the silver wire as well as the length of silver wire coated with hydrogel is kept constant for all the electrodes fabricated.

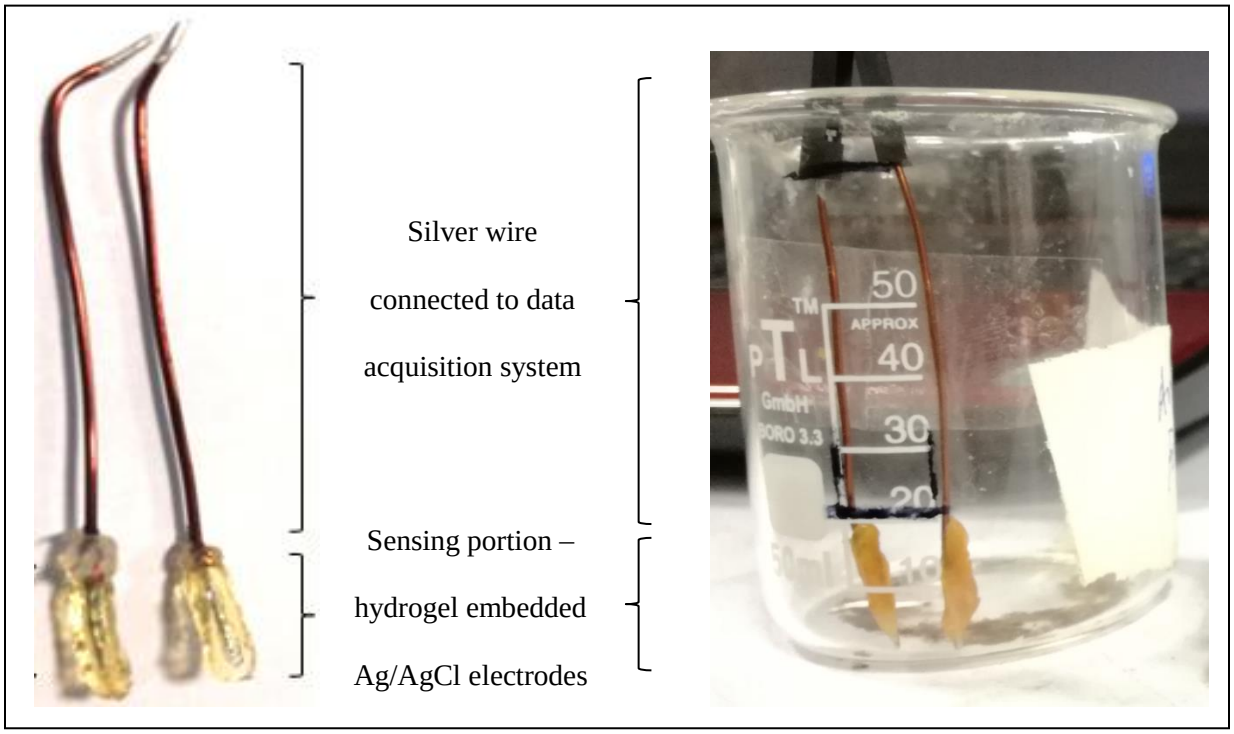


Figure 3.3: Sensor Fabrication

3.6.2 Sensor Testing

The selected hydrogel compositions that showed the desired mechanical stability characteristics and that showed good results as far as the thermo-gravimetric testing is concerned were further shortlisted for the hydrogel based temperature sensor testing. The swelling behavior of the hydrogels was measured once immersed in PECF solution at different temperatures.

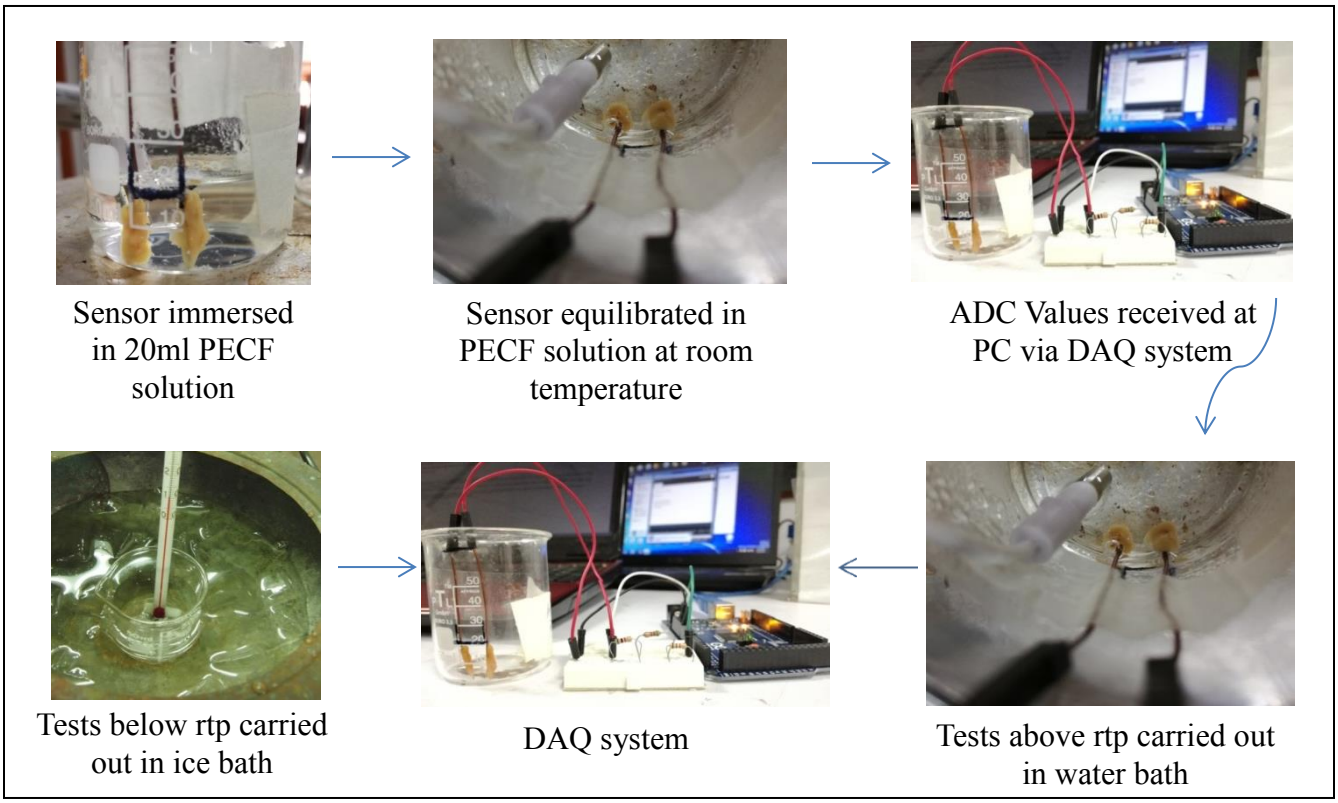


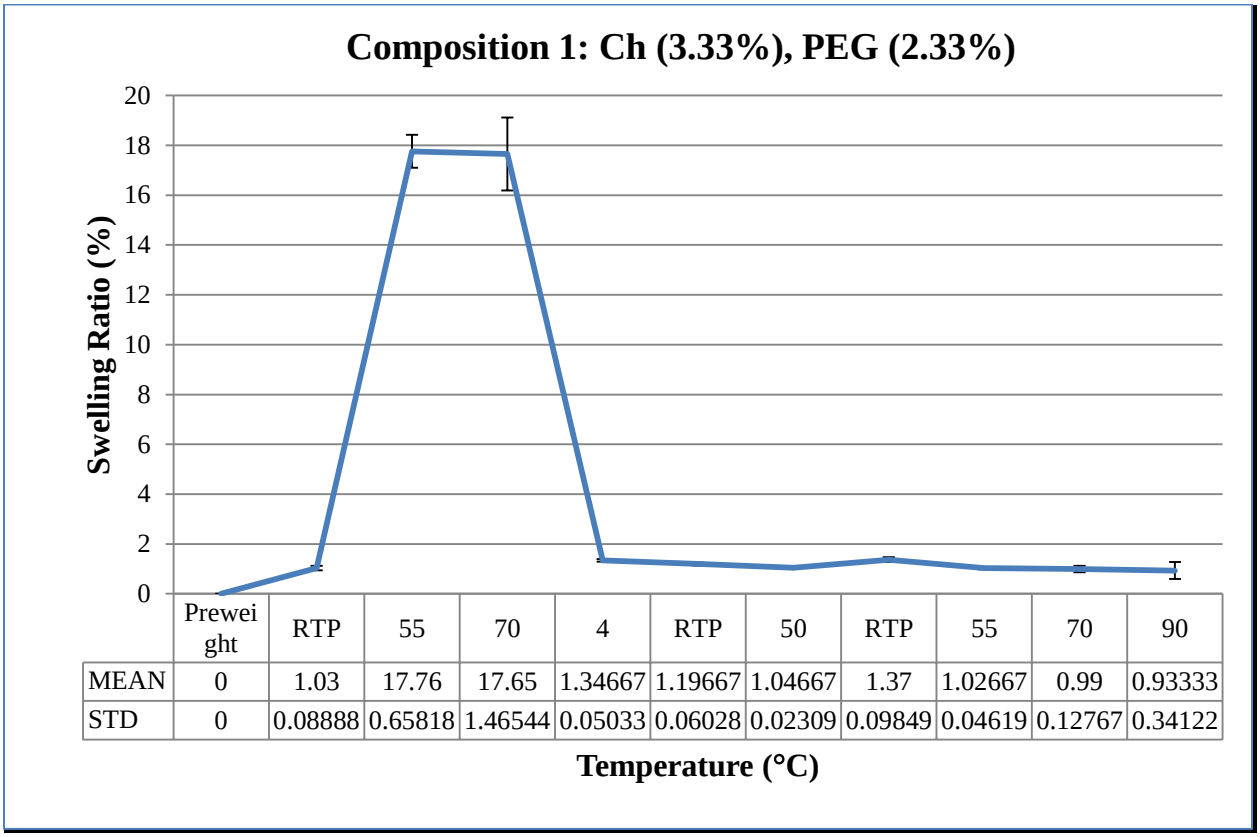
Figure 3.4: Experiment Protocol for Hydrogel based Sensor Testing

Each hydrogel based sensor was immersed in 20ml PECF solution in a beaker. Each of these sensors was first equilibrated in PECF solution at room temperature. The sensor was kept in an unchanged state until the ADC values received at the PC via the Data Acquisition (DAQ) system maintained a constant value for at least 5 minutes. Once this exercise had completed, the sensors were exposed to different temperature values by placing the beaker containing the sensor system in water baths maintained at various temperatures. A heated water bath served the purpose of providing exposure to the sensors at above room temperature upto 70°C while an ice bath was made use of when temperatures below room temperature are required. The ADC values were noted down alongside the exposure temperature.

CHAPTER 4 RESULTS AND DISCUSSION

4.1. Hydrogel Thermo-gravimetric Testing (Volume Phase Transition behavior)

Time dependent swelling behaviors of the hydrogels in PECF solution at different temperatures have been plotted. All the hydrogels swelled rapidly and reached equilibrium at room temperature after which they were exposed to various temperature values which are mentioned in the plots. The swelling behavior plotted in these figures is the average of three samples.

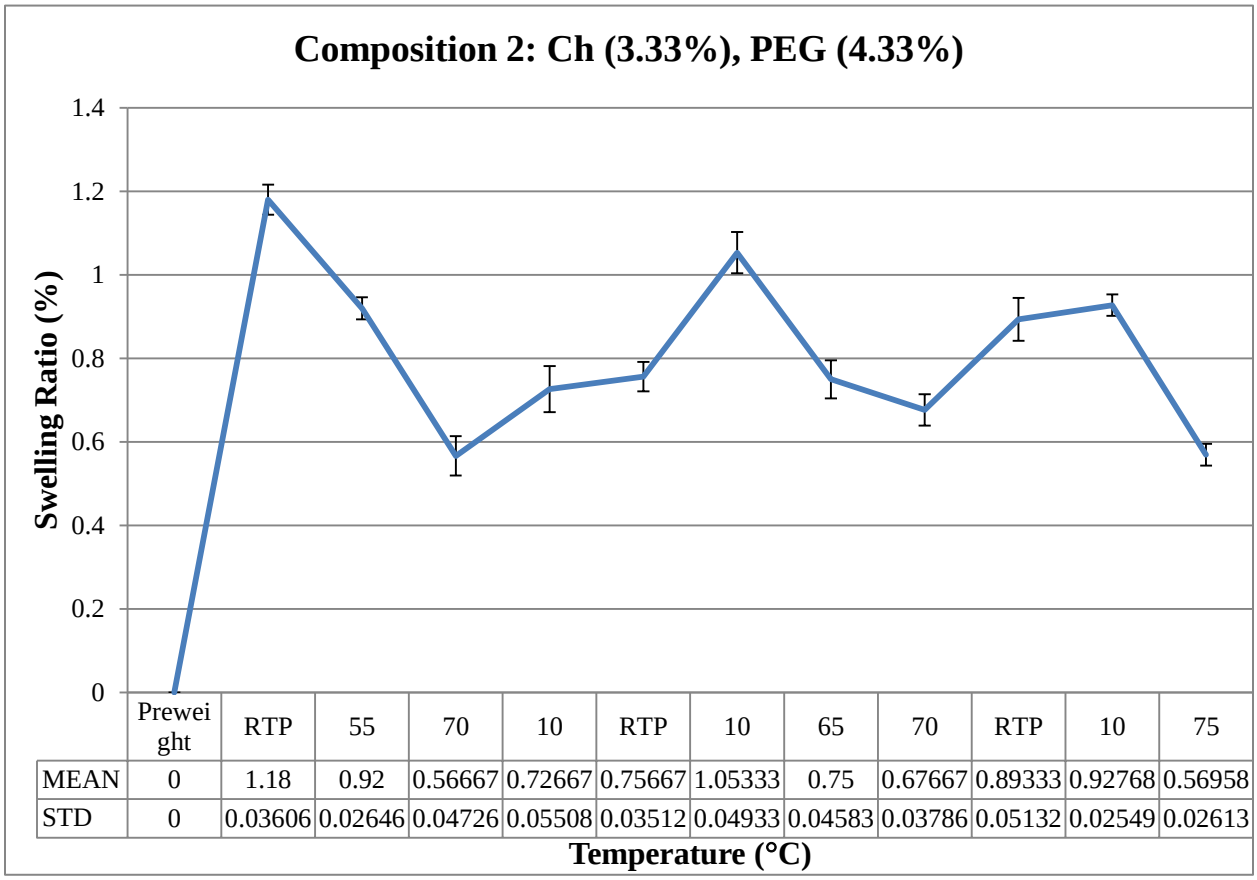


	Preweight	RTP	55	70	4	RTP	50	RTP	55	70	90
MEAN	0	1.03	17.76	17.65	1.34667	1.19667	1.04667	1.37	1.02667	0.99	0.93333
STD	0	0.08888	0.65818	1.46544	0.05033	0.06028	0.02309	0.09849	0.04619	0.12767	0.34122

Figure 4.1: Composition 1: Ch (3.33%), PEG (2.33%)

Composition 1 has a 3 to 2 ratio of Chitosan to PEG. It is observed to give one time response. It can also be seen from the trend visible in Figure 4.1 that the hydrogel appears to have degraded after being exposed to a temperature as high as 70°C. This is the reason behind the huge error bar that appears corresponding to 70°C. Moreover, composition 1 in comparison

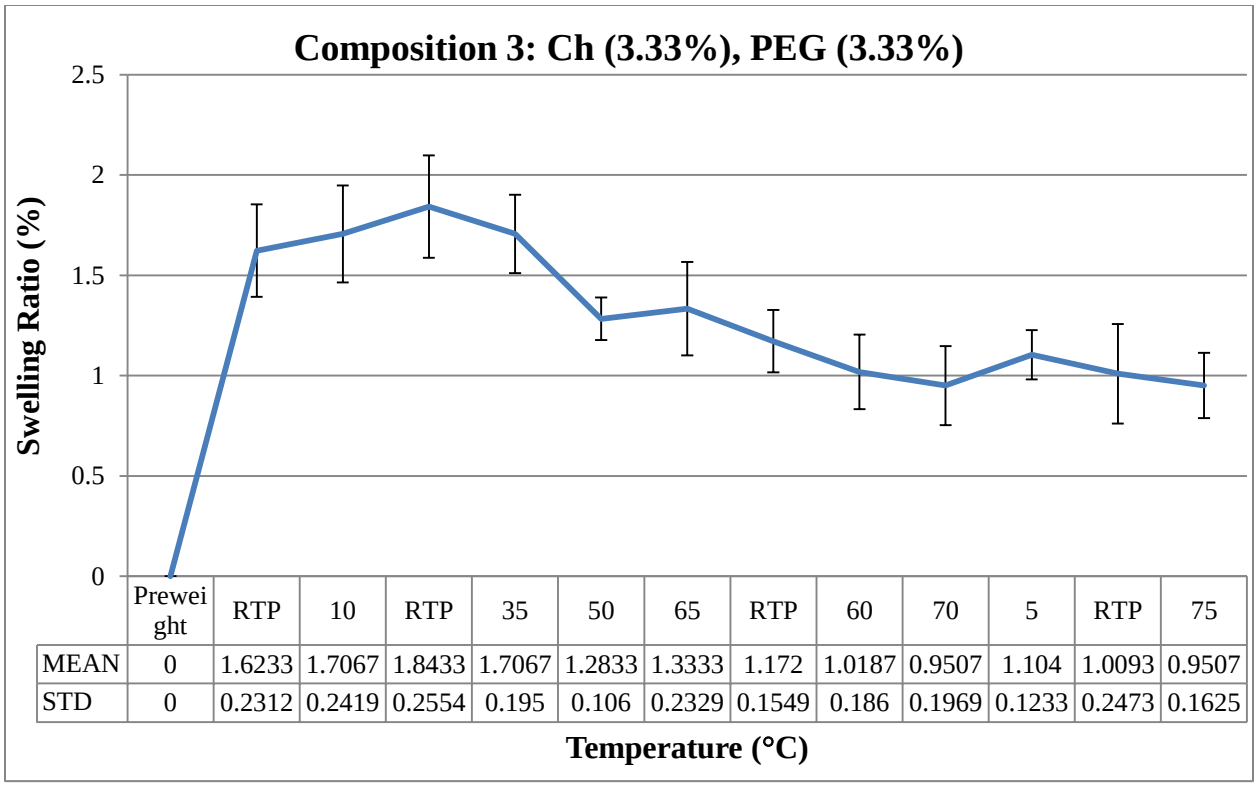
to all the other compositions, gives maximum swelling on exposure to different temperatures. It gives a maximum swelling ratio valued 17.76%, which is way greater than that observed for other compositions.



	Preweight	RTP	55	70	10	RTP	10	65	70	RTP	10	75
MEAN	0	1.18	0.92	0.56667	0.72667	0.75667	1.05333	0.75	0.67667	0.89333	0.92768	0.56958
STD	0	0.03606	0.02646	0.04726	0.05508	0.03512	0.04933	0.04583	0.03786	0.05132	0.02549	0.02613

Figure 4.2: Composition 2: Ch (3.33%), PEG (4.33%)

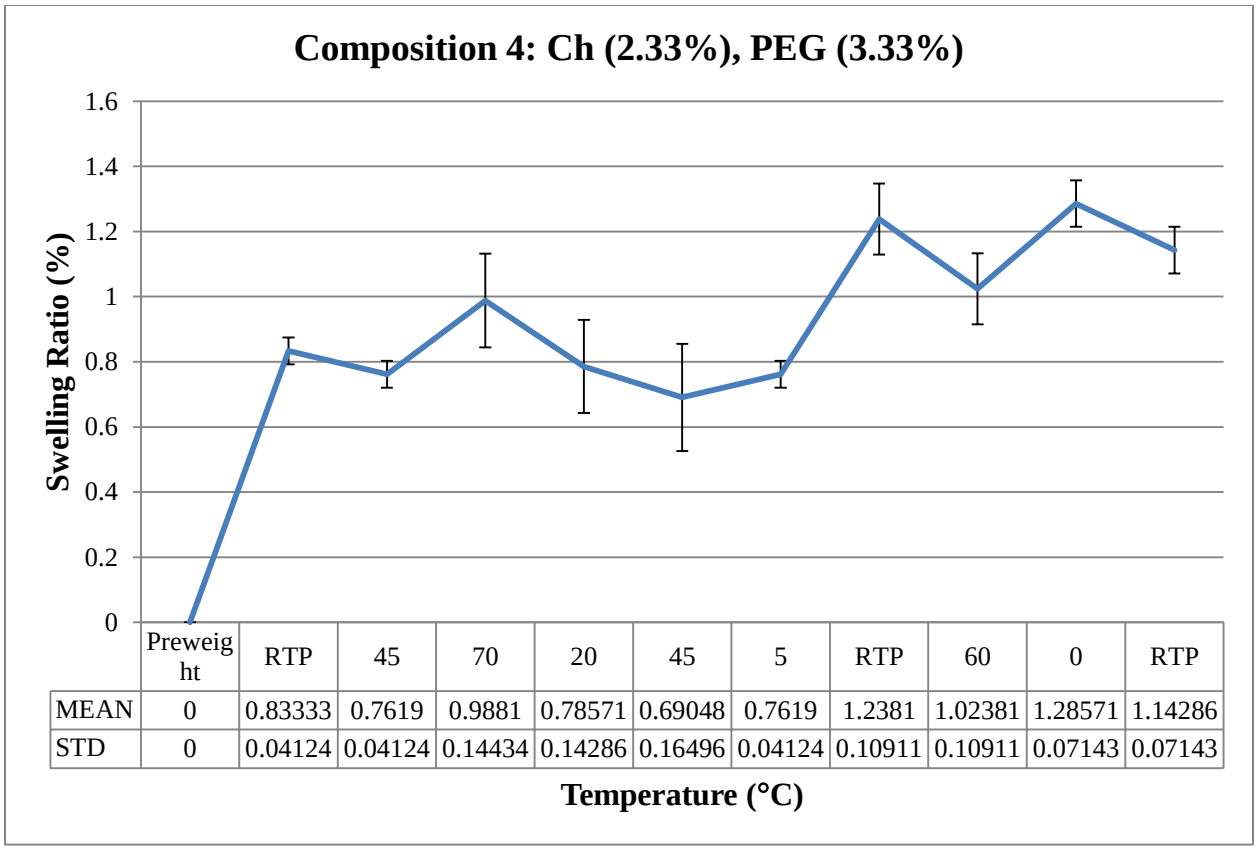
Composition 2 appears to give a reversible swelling trend on exposure to different temperatures. This composition gave the most suitable results, closest to the desired characteristics. Although it gave smaller swelling ratio values, it did fulfill the requirement of thermal reversibility.



	Preweight	RTP	10	RTP	35	50	65	RTP	60	70	5	RTP	75
MEAN	0	1.6233	1.7067	1.8433	1.7067	1.2833	1.3333	1.172	1.0187	0.9507	1.104	1.0093	0.9507
STD	0	0.2312	0.2419	0.2554	0.195	0.106	0.2329	0.1549	0.186	0.1969	0.1233	0.2473	0.1625

Figure 4.3: Composition 3: Ch (3.33%), PEG (3.33%)

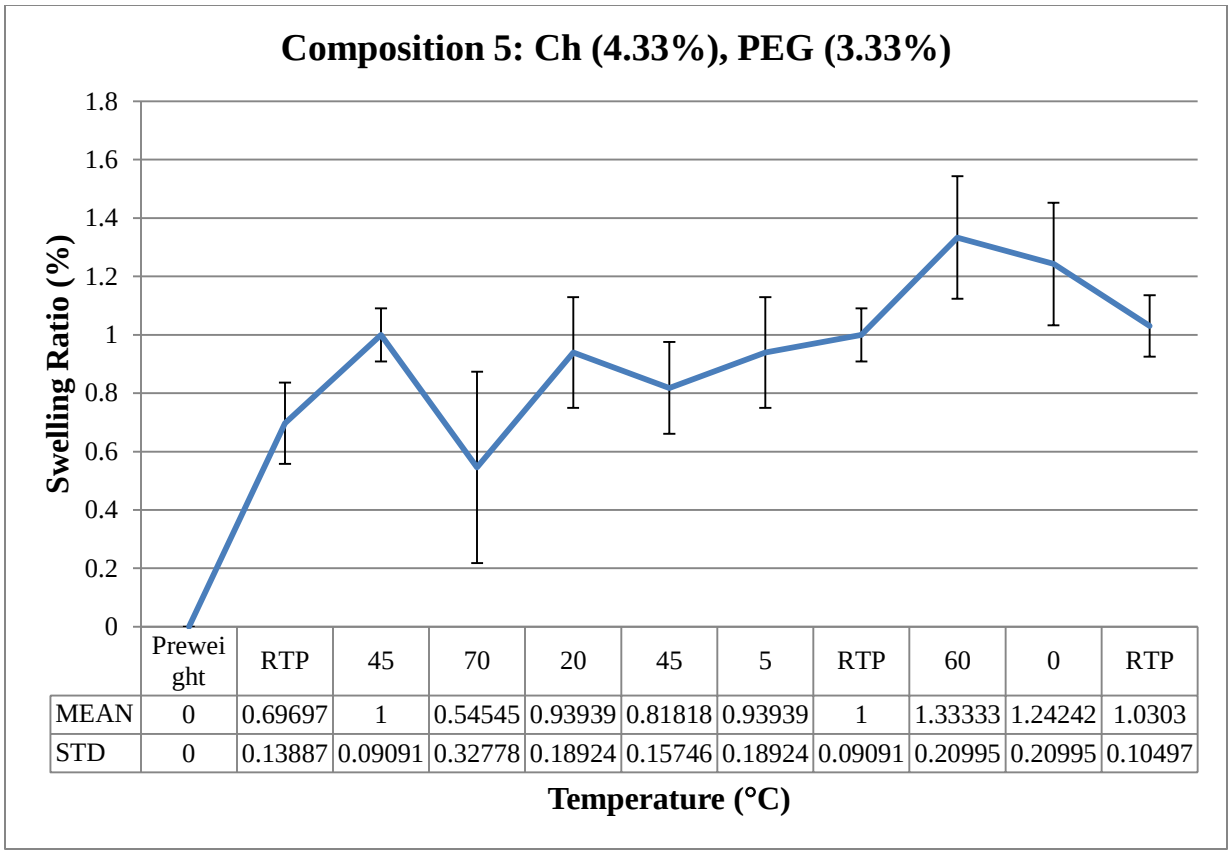
This composition comprises of Chitosan and PEG in a 1 to 1 ratio. The trend in Figure 4.3 suggests a degradation of hydrogel's thermoresponsive characteristics. It shows a constantly decreasing trend with very little reversibility. The swelling ratios are not large enough either. There is an almost constant error observed throughout the course of this experiment.



	Preweight	RTP	45	70	20	45	5	RTP	60	0	RTP
MEAN	0	0.83333	0.7619	0.9881	0.78571	0.69048	0.7619	1.2381	1.02381	1.28571	1.14286
STD	0	0.04124	0.04124	0.14434	0.14286	0.16496	0.04124	0.10911	0.10911	0.07143	0.07143

Figure 4.4: Composition 4: Ch (2.33%), PEG (3.33%)

Composition 4 has a 2 to 3 ratio of Chitosan to PEG. The trend appears to be repeating but an overall constantly increasing shift is seen too. The resulting swelling ratios have small values and greater error value is observed.



	Preweight	RTP	45	70	20	45	5	RTP	60	0	RTP
MEAN	0	0.69697	1	0.54545	0.93939	0.81818	0.93939	1	1.33333	1.24242	1.0303
STD	0	0.13887	0.09091	0.32778	0.18924	0.15746	0.18924	0.09091	0.20995	0.20995	0.10497

Figure 4.5: Composition 5: Ch (4.33%), PEG (3.33%)

Composition 5 gives an overall increasing trend with very high error values. No repeatability is seen in the trend, although, as with all the other compositions, it is the resultant mean graph of experiments with 3 different samples having the same geometry.

As a conclusion to the thermo-gravimetric testing results, composition 2 seems to be the strongest candidate, because it potentially appears to be the most sensitive and thermally reversible hydrogel among all the other tested combinations.

4.2. Characterization of Hydrogels

4.2.1 Chemical Structure Analysis

FTIR was carried out on the fresh and exposed hydrogel samples for each of the 3 shortlisted compositions and the results obtained are as under:

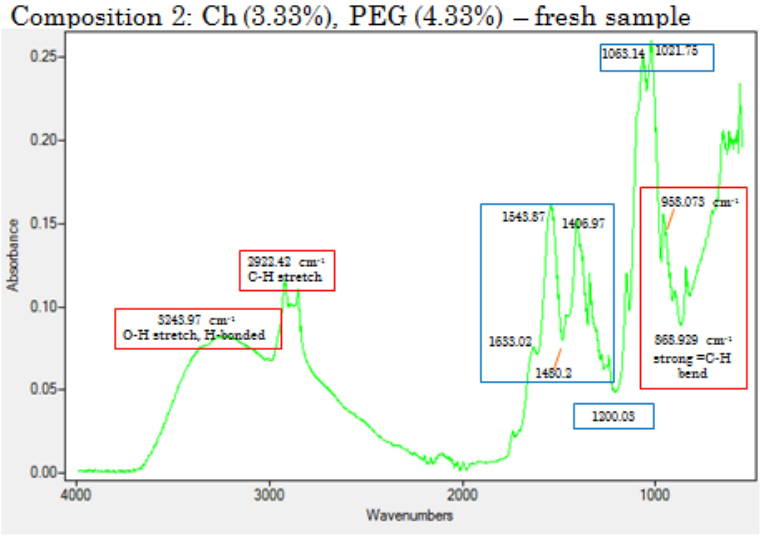


Figure 4.6: FTIR Composition 2: Ch (3.33%), PEG (4.33%) – fresh sample

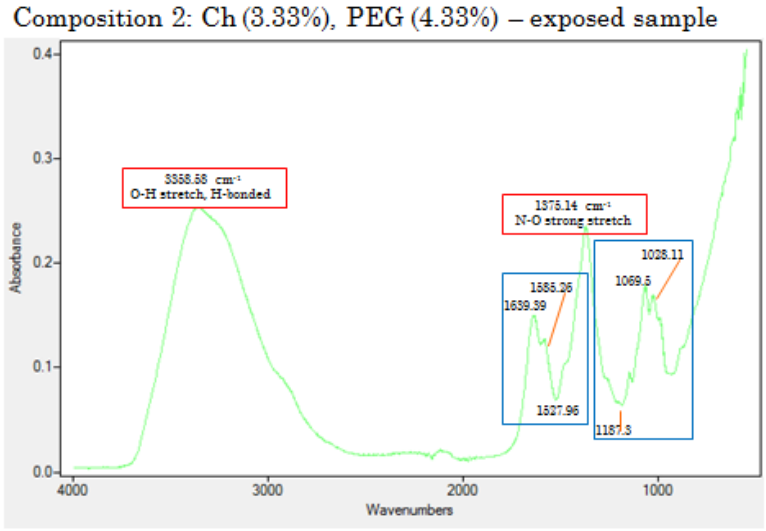


Figure 4.7: FTIR Composition 2: Ch (3.33%), PEG (4.33%) – exposed sample

The Left Hand Side represents the peaks characteristic of Chitosan. It can be clearly seen from the comparison of Figure 4.6 and 4.7 that the Chitosan's C-H stretch degrades on exposure to varying temperatures.

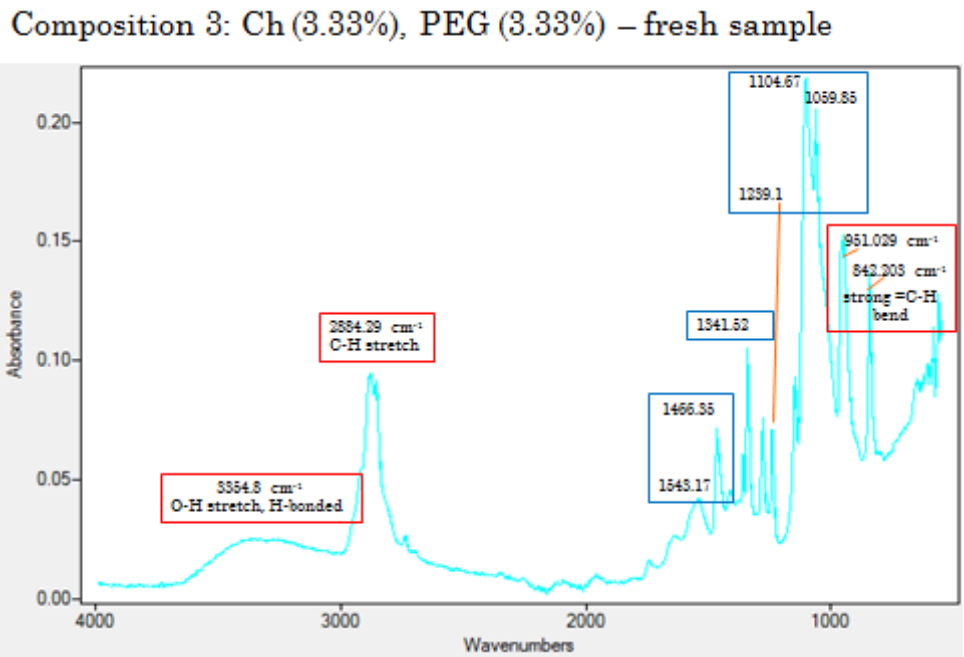


Figure 4.8: FTIR Composition 3: Ch (3.33%), PEG (3.33%) – fresh sample

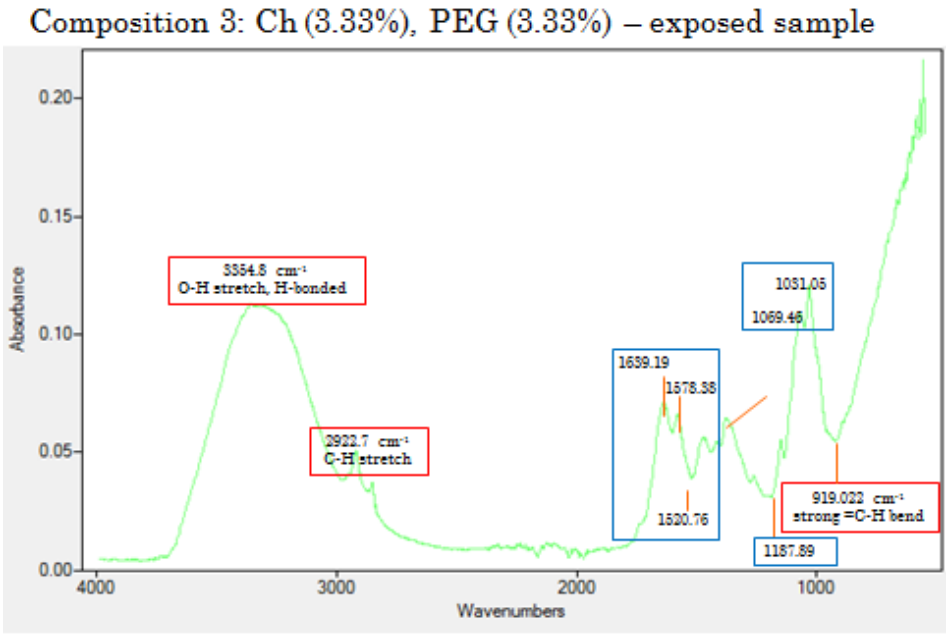


Figure 4.9: FTIR Composition 3: Ch (3.33%), PEG (3.33%) – exposed sample

Shallower peaks here depict a changed interaction as compared to that observed for composition 2.

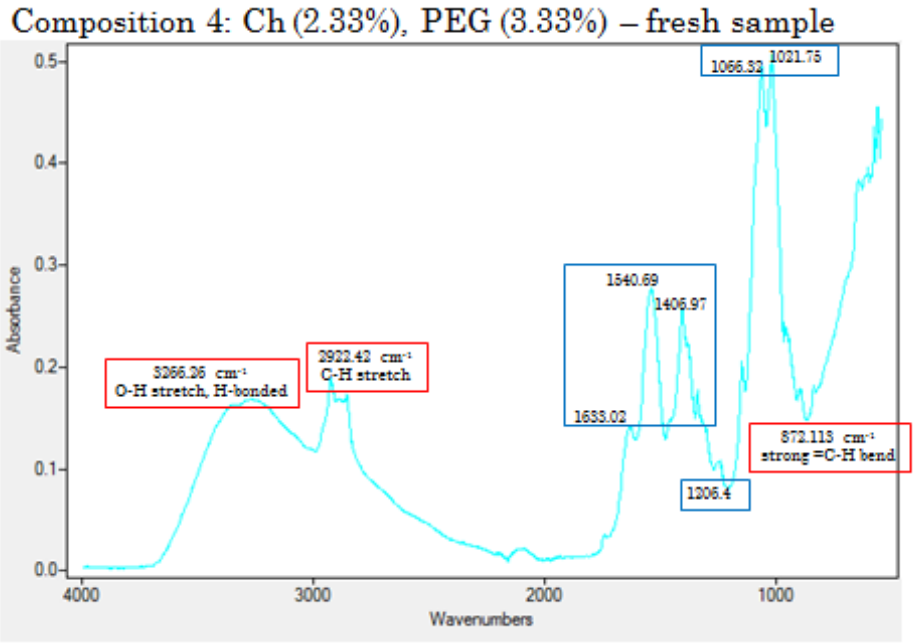


Figure 4.10: FTIR Composition 4: Ch (2.33%), PEG (4.33%) – fresh sample

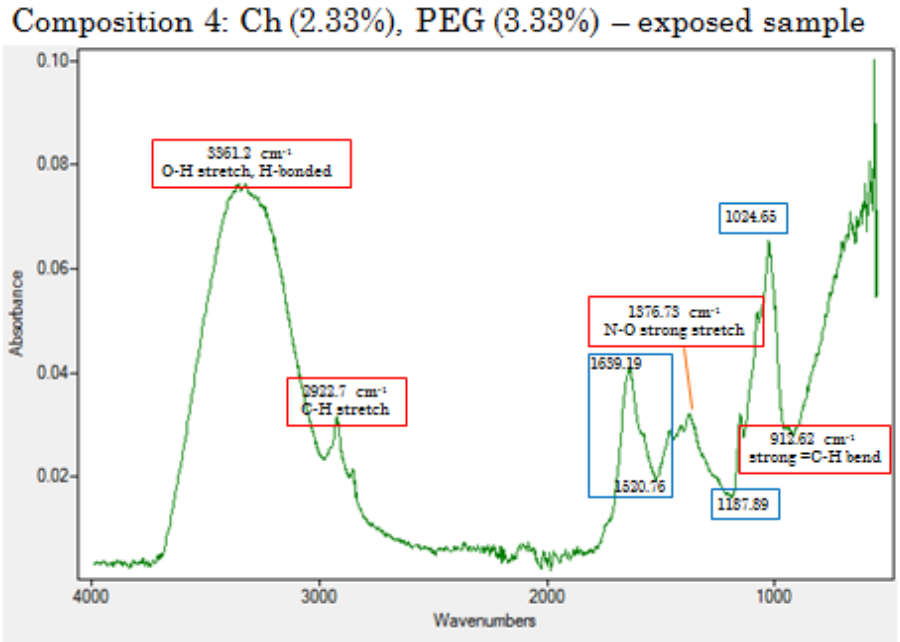


Figure 4.11: FTIR Composition 4: Ch (2.33%), PEG (3.33%) – exposed sample

All these results from the FTIR show the presence of an intermolecular interaction between chitosan and polyethylene glycol, as documented. [23] Therefore, the intermolecular

interaction between chitosan and PEG can be attributed to the hydrogen bond. This means that it is the hydrogen bond interaction between chitosan and PEG that leads to the O-H stretching vibrations. O-H band increases in intensity and becomes broader in exposed samples. This tells that bonds have broken down and water content has raised. Even after drying, water content hasn't completely finished.

Moreover, it can also be observed from comparison of figure 4.6 to 4.11 that with increasing content of PEG, the O-H stretching vibrations appear to have greater strength.

4.2.2 Crystallographic Analysis

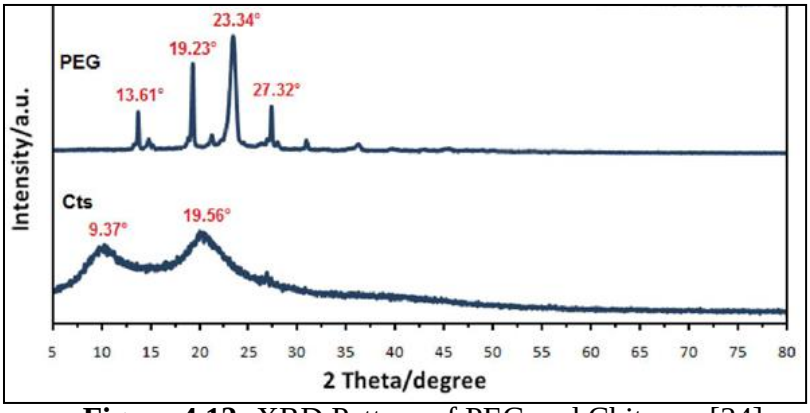


Figure 4.12: XRD Pattern of PEG and Chitosan [24]

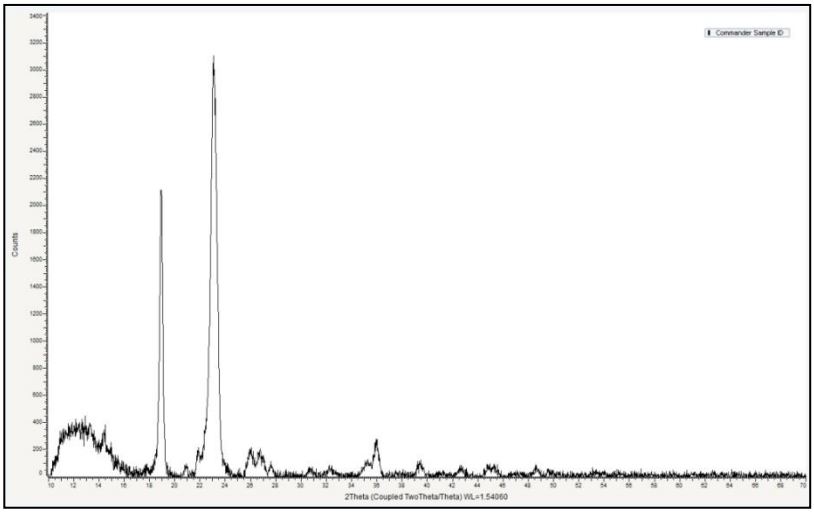


Figure 4.13: XRD Pattern for Chitosan-PEG Hydrogel

Pure Chitosan, as shown on Figure 4.12 shows two peaks at 2θ of 9.37° and 19.56° while pure PEG shows strong reflections at 2θ of 19.23° and 23.34° and weak reflections at 13.61° and 27.32°. The diffraction of PEG tends to cover the reflection of chitosan with increasing reflection

at 19.13° in Chitosan/PEG hydrogel, as can be seen in Figure 4.13. The hydrogel shows strong reflections at 2θ of 19.13° and 23.20°. The reflection for chitosan appears to be diminished indicating that the crystallinity of chitosan is reduced.

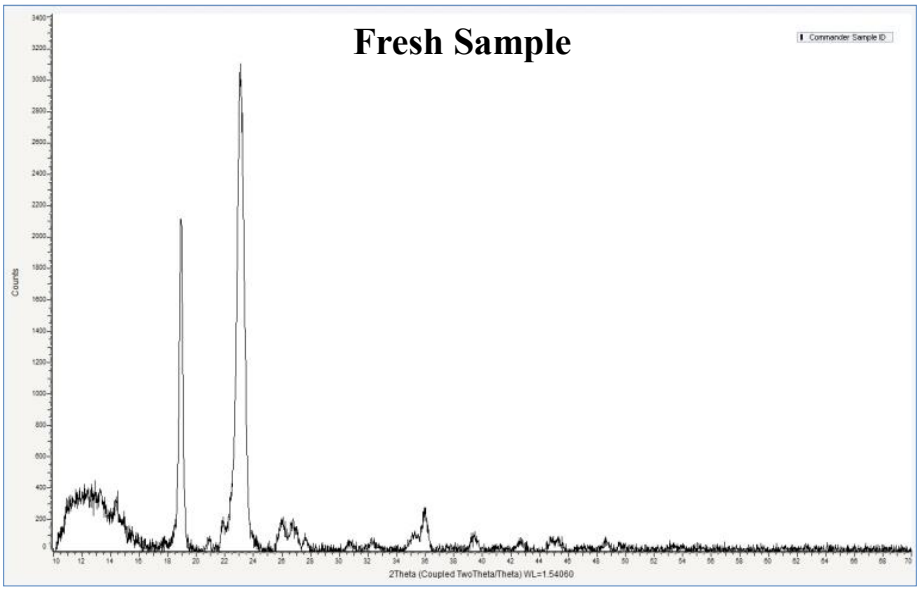


Figure 4.14: XRD Pattern – fresh sample

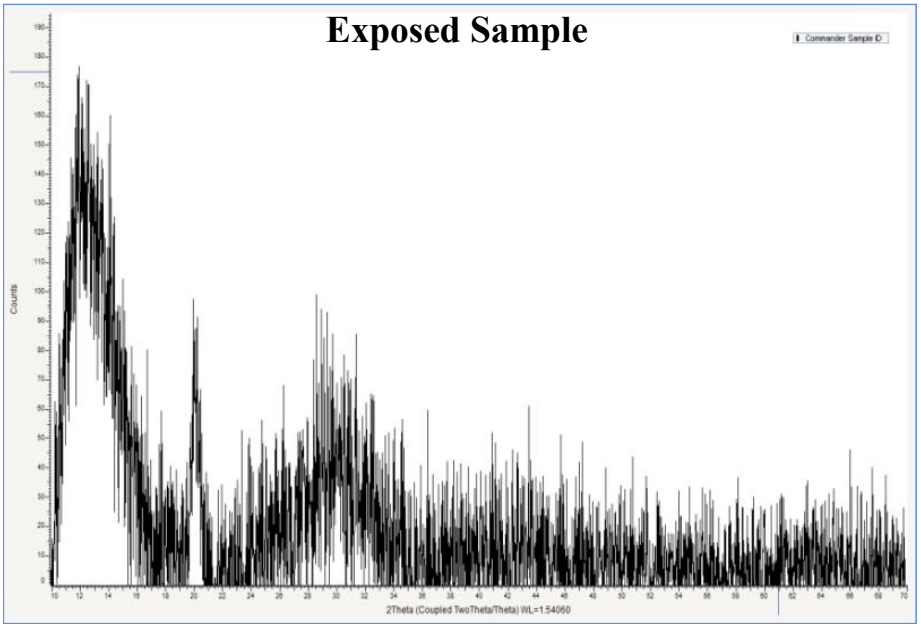


Figure 4.15: XRD Pattern – exposed sample

In the pattern obtained for unexposed or fresh sample shown in figure 4.14, there is greater crystallinity observed which is depicted by the presence of sharper or narrower peaks. On the other hand, in case of exposed sample (Figure 4.15), the peaks appear to be broader, or not as

sharp as fresh sample because they have taken up the fluid in the shape of PECF to which the hydrogels were exposed. So the sample no longer possesses crystalline configuration. It has become amorphous in nature, on exposure to the solvent at different temperatures.

The XRD results agree to the observations made in FTIR analysis. The hydrogel molecular structure changes right after exposure to PECF and temperature change. Furthermore, the hydrogen bond interaction between chitosan and PEG restrains the movement of chitosan molecules and even partially destroys the original crystalline structure of chitosan, and consequently decreases chitosan crystallization upon blending.

4.2.3 Surface Morphological Analysis

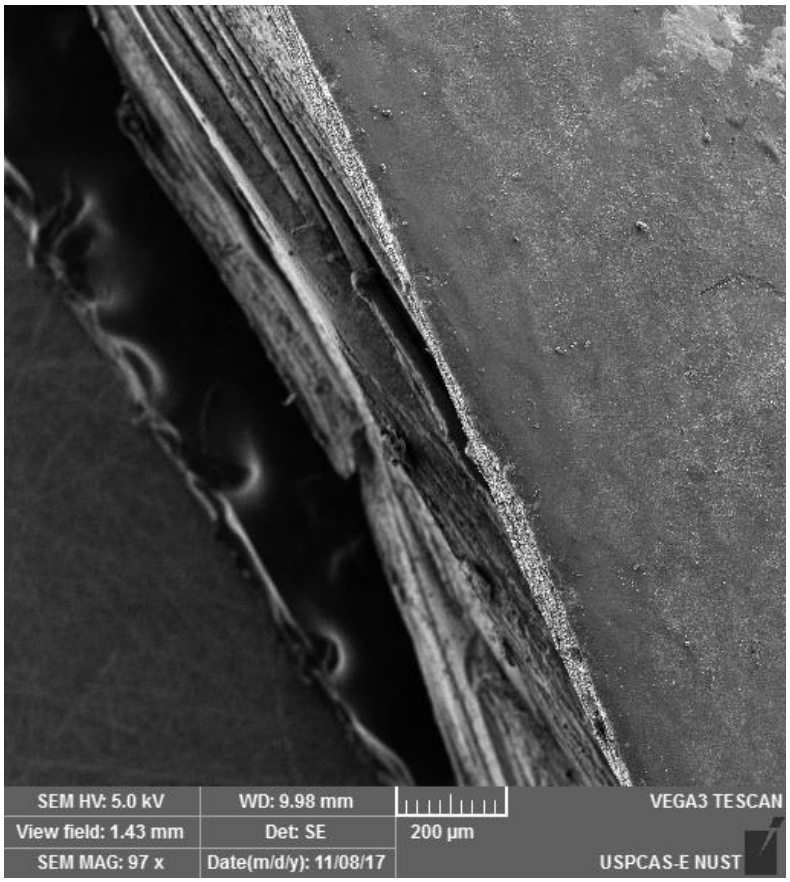


Figure 4.16: SEM Composition 2: Ch (3.33%), PEG (4.33%) – fresh sample

Figure 4.16 displays closely and regularly packed layers before exposure to PECF and temperature change, which appear not to be very pervious to the solvent. PEG became a key

influencing factor due to the crystalline nature of PEG and to the effect of chitosan on PEG. Consequently, the SEM analysis of the hydrogel film shows fine regularly packed layered structure.

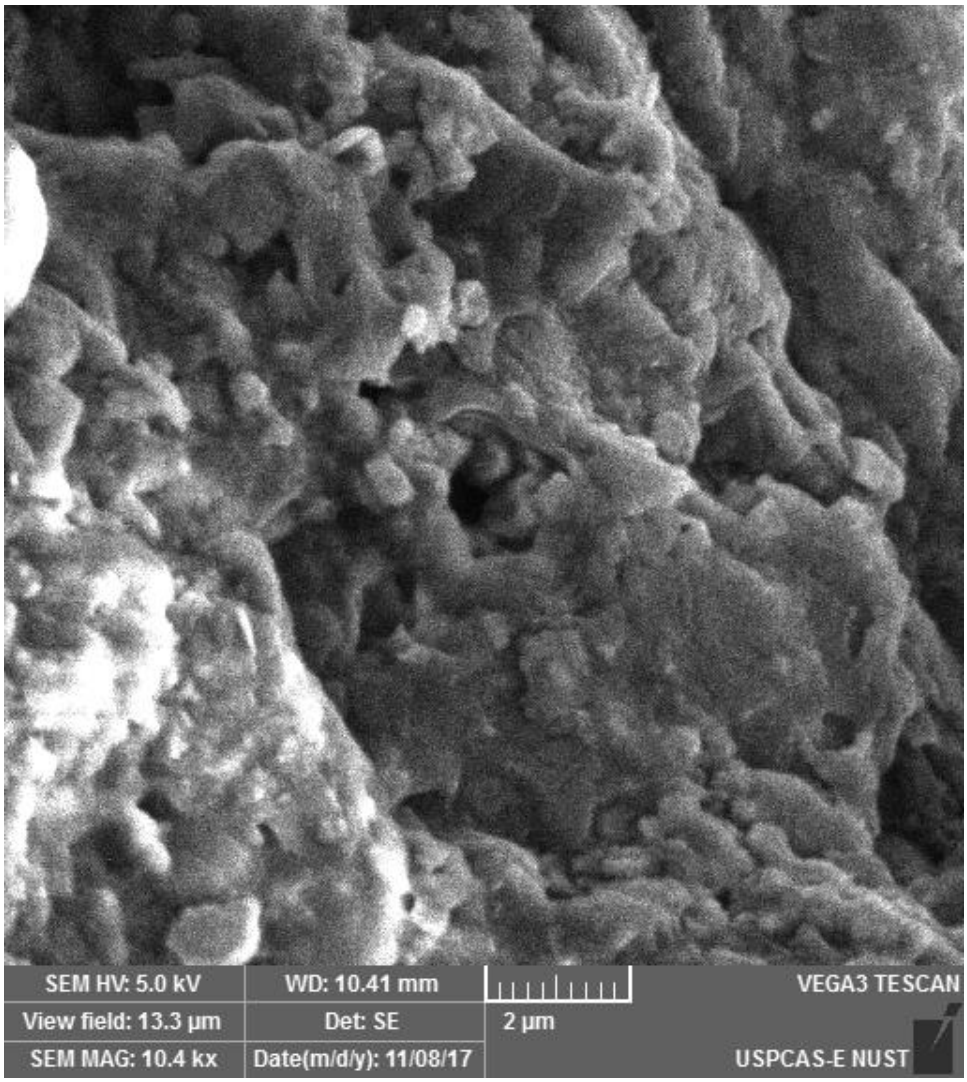


Figure 4.17: SEM Composition 2: Ch (3.33%), PEG (4.33%) – exposed sample

Figure 4.17 shows pores that are clearly visible post exposure to PECF and varying temperature. It appears to be a non-stratified structure, tightly woven, little pitting, which points towards the 3D polymeric structure of the blend and lastly, irregularity that gives an indication of amorphous structure of the exposed hydrogel.

4.3. Hydrogel based Temperature Sensor Testing

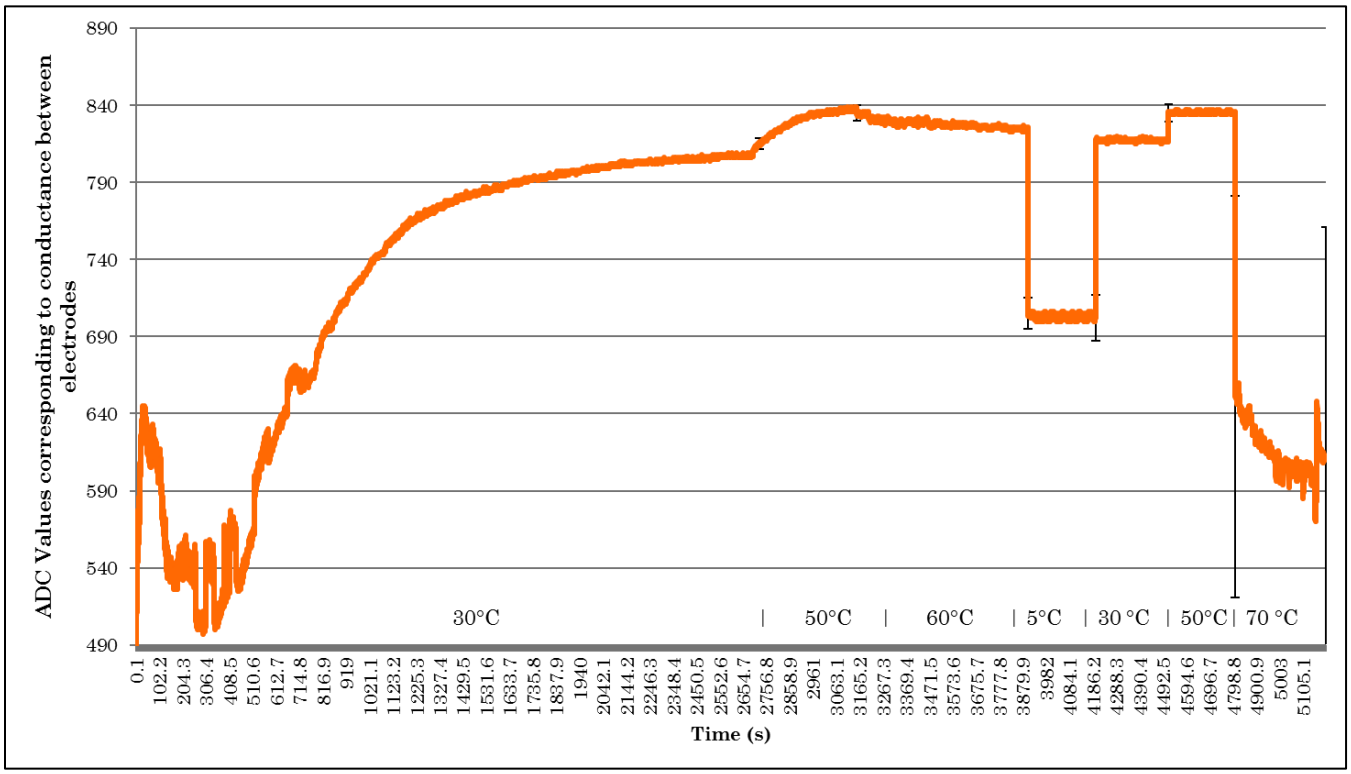


Figure 4.18: Sensor Testing - Composition 2: Ch (3.33%), PEG (4.33%)

This coincides with the result obtained in the thermo-gravimetric testing of the hydrogel samples because the same composition appeared to have degraded at 70°C. The sensor appears to go through the same behavior when exposed to PECF solution at 70°C.

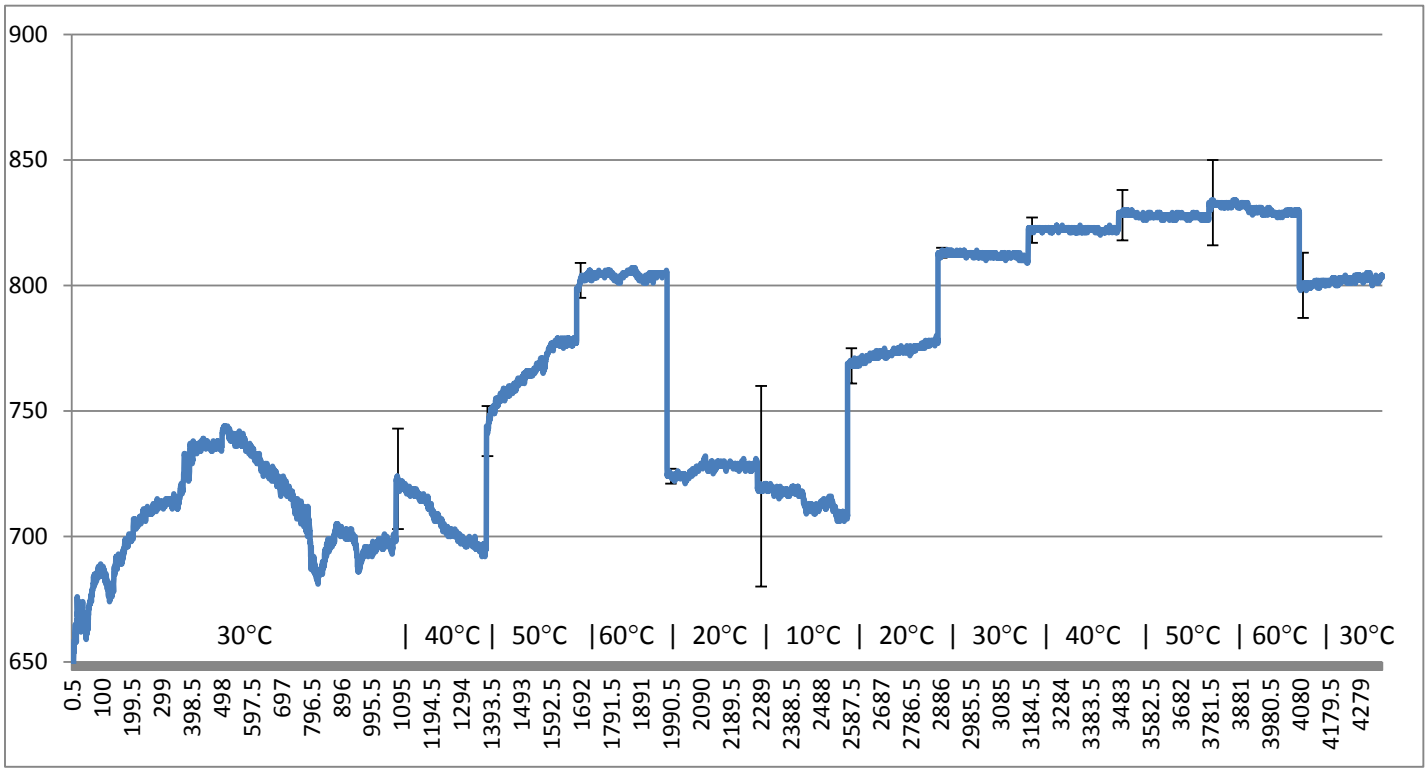


Figure 4.19: Sensor Testing - Composition 3: Ch (3.33%), PEG (3.33%)

The composition 3 shows better results in sensor testing as far as sensitivity to temperature change is concerned. It also appears to have near to reversible characteristics, although an overall increasing trend is observed.

CHAPTER 5 CONCLUSION AND FUTURE PERSPECTIVES

A thermally responsive hydrogel comprising of Chitosan and Polyethylene glycol (PEG) is synthesized and fully characterized. It offers potential to be used as a temperature responsive hydrogel based sensor thus overcoming the problems with conventional temperature sensors such as lacking flexibility, inappropriate size etc.

However, the toxicity of the crosslinker used in the making of the proposed hydrogel, i.e. glutaraldehyde has adverse effects on the biocompatibility of the used materials. Thus, the crosslinker has to be replaced by nontoxic and biocompatible agents. One feasible alternative is genipin, a natural crosslinking agent which is much less toxic compared to glutaraldehyde. Genipin readily crosslinks polymers containing amino groups and the crosslinking mechanism has been well described by Butler et al [25].

In addition to this, the proposed composition can be gelatinized. This is expected to present enhanced swelling/deswelling ability and better structural integrity.

Lastly and most importantly, the usage of the proposed hydrogel can be explored in other medical applications, making use of its thermal responsivity, sensitivity and reversibility.

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