HYDROGEL FROM TEMPLATE POLYMERIZATION OF METHACRYLIC ACID AND N-VINYLPYROLLIDONE AND POLYETHYLENEOXIDE

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APRIL 2005

Approval of the Graduate School of Natural and Applied Sciences

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I certify that this thesis satisfies all the requirements as a thesis for the degree of Master of Science.

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This is to certify that we have read this thesis and that in our opinion it is fully adequate, in scope and quality, as a thesis for the degree of Master of Science.

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ABSTRACT

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This theses covers the preparation and the characterization of a rigid hydrogel from N-Vinyl pyrrolidone-methacrylic acid (VP-MAA) monomers and polyethyleneoxide (PEO) polymer.

Hydrogels are hydrophillic natured three dimensional networks which can swell in the presence of water. The VP-MAA-PEO hydrogel was obtained by template polymerization which can be defined as a method of polymer synthesis in which specific interactions consists of the preparation of a polymer (daughter polymer) in the presence of a macromolecular compound (template polymer).

The hydrogel of VP-MAA-PEO was synthesized by using azobisisobutyronitrile (AIBN) as the initiator, tetrahydrofurane (THF) as the solvent and the temperature of the system was kept constant at 50ºC. Two kinds of VP-MAA-PEO hydrogels were prepared. The only difference between them were their solubilities in water. This difference is due to

different crosslinking agent weight percentages of ethylene glycol dimethacrylic (EGDMA) to make the hydrogel water insoluble.

The comparison of two hydrogels were carried by swelling behaviors at different pH values and different temperatures. Thermal stability of these two hydrogels were also examined by differential scanning calorimetry (DSC), spectroscopic properties were compared by using FTIR spectrometer and morphological studies were analyzed by using scanning electron microscope (SEM).

Keywords: template polymerization, hydrogel, methacrylic acid, vinyl pyrrolidone, polyethyleneoxide

ÖZ

METAKRİLİK ASİT VE N-VİNİL PİROLİDON VE POLİETİLEN OKSİTTEN ŞABLON POLİMERİZASYONU İLE HİDROJEL YAPIMI

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Bu tez N-Vinil pirolidon ve metakrilik asit (VP-MAA) monomerleri ile polietilenoksit (PEO) polimerinden sert hidrojel hazırlanması ve karakterizasyonunu kapsamaktadır.

Hidrojeller, hidrofilik yapıda olan, üç boyutlu, sulu ortamlarda şişebilen yapılardır. VP-MAA-PEO hidrojeli şablon polimerizasyon yöntemi kullanılarak hazırlandı. Şablon polimerizasyonu makromoleküler madde (şablon polimeri) varlığında polimer (kardeş polimer) hazırlanmasını içeren bir polimer sentezleme yöntemidir.

VP-MAA-PEO hidrojeli azobisizobütironitril (AIBN) başlatıcı olarak kullanılarak, tetrahidrofuran (THF) çözücüde ve 50°C sabit sıcaklıkta sentezlendi. Bu çalışmada iki çeşit VP-MAA-PEO hidrojeli hazırlandı. İki hidrojel arasındaki tek fark bunların sudaki çözünürlükleri ve çapraz

bağlayıcı ağırlık yüzdeleridir. Çapraz bağlayıcı olarak etilen glikol dimetakrilat (EGDMA) monomeri kullanıldı.

Hazırlanan bu iki hidrojelin karşılaştırması deneysel olarak yapıldı. Şişme özellikleri farklı pH değerlerinde ve farklı sıcaklık değerlerinde analiz edildi. Isıl kararlılıkları Diferansiyel Taramalı Kalorimetre (DSC) kullanılarak çalışıldı. Spektroskopik analizler FTIR spektrometresi ve morfolojik çalışmalar Taramalı Elektron Mikroskopisi kullanılarak yapıldı.

Anahtar Kelimeler: şablon polimerizasyonu, hidrojel, metakrilik asit, vinil pirolidon, polietilenoksit

TO MY FAMILY

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ABBREVIATIONS

VP :	Vinyl Pyrrolidone
MAA :	Methacrylic acid
PEO :	Polyethylene oxide
HA :	Hydroxyapatite
EGDMA :	Ethylene glycol dimethacrylate
XL :	Crosslinking agent
VP-MAA-PEO :	Vinyl Pyrrolidone - Methacrylic acid - Polyethylene oxide
AIBN :	α,α'- Azoisobutyronitrile
THF :	Tetrahydrofuran
LXL :	Low amount of Crosslinking agent
HXL :	High amount of Crosslinking agent
ES :	Equilibrium swelling

CHAPTER 1

INTRODUCTION

1.1. Synthetic polymers as biomaterials

Biomaterial is defined as any substance (other than a drug) or combination of substances synthetic or of natural origin, which can be used for any period of time, as a part of a system which treats, augments, or replaces any tissue, organ, or function of the body [1,2]. There are three principle categories of solid biomaterials. They are metals, polymers and ceramics. Since the structures of these materials differ, they have different properties and, therefore, different uses in the body.

Metallic biomaterials are classified as nearly inert materials. Because of their mechanical strength (high tensile and fatique strength) and biocompatibility, metals are superior in load-bearing implants such as hip and knee prostheses and fracture fixation wires, pins, screws, and plates. Although pure metals are sometimes used, alloys (metals containing two or more elements) frequently provide improvement in material properties, such as strength and corrosion resistance [3]. The main considerations in selecting metals and alloys for biomedical applications are biocompatibility, appropriate mechanical properties, corrosion resistance, and reasonable cost. The physiological environment is typically modelled as 37ºC aqueous solution, at pH 7.3, with dissolved gases (such as oxygen), electrolytes, cells, and proteins. Immersion of metals in this environment can lead to corrosion which lead to reduce the biocompatibility of materials. The electrochemical reactions that lead to corrosion are reduced or prevented. In fact, the stability of the oxides

present in different metals determines their overall corrosion resistance.

Ceramics are materials composed of metallic and non-metallic elements held together by ionic and/or covalent bonds. As with metals, the interatomic bonds in ceramics result in long-range three-dimensional crystalline structures. Ceramics are typically electrical and thermal insulators. The strong ionic and covalent bonds also make ceramics hard and brittle.

The ionic and covalent nature of ceramics also influences their chemical behaviour [4]. Although they do not undergo corrosion, ceramics are susceptible to other forms of degradation when exposed to the physiological environment. Bioceramics are classified into bio inert and bioactive ceramics. Bioactive ceramics are also degraded in the body. Not only can they undergo slow or rapid dissolution but because of the similarity of calcium phosphates to the mineral component of bone, they may also be resorbed by osteoclasts (the cells that break down bone). The major drawbacks to the use of ceramics are their brittleness and poor tensile properties, although they can have outstanding strength when loaded in compression. Bioactive ceramics include synthetic HA, tricalcium phosphate and bioactive glass-ceramics are use for artificial bone. Bioactive ceramic coatings of metals have been developed to overcome the disadvantage of both metal and bioactive ceramic and excellent clinical results are reported in short term [5]. Some kinds of ceramics used in Biomedical Applications and their kinds are mentioned below.

Table 1 Ceramics Used in Biomedical Applications [4]

CERAMIC	**KIND**
Alumina	Bioinert
Zirconia	Bioinert
Pyrolitic Carbon	Bioinert
Hydroxyapatite	Bioactive
Tricalcium Phosphate	Biodegradable

The definitions mentioned, where they are used in biomedical applications in all respects above, are the followings;

Bioinert: refers to a material that retains its structure in the body after implantation and does not induce any immunologic host reactions.

Bioactive: refers to materials that form bonds with living tissue.

Biodegradable: refers to materials that degrade in the body while they are being replaced by regenerating natural tissue; the chemical by products of the degrading materials are absorbed and released via metabolic processes of the body.

Polymers are the most widely used materials in biomedical applications, such as cardiovascular devices as well as for replacement and augmentation of various soft tissues, in drug delivery systems, in diagnostic aids, and as a scaffolding material for tissue engineering applications. The mechanical and thermal behaviour of polymers are influenced by several factors, including the composition of the backbone and side groups, the structure of the chains, and the molecular weight of the molecules.

Plastic deformation occurs when the applied mechanical forces cause the macromolecular chains to slide past one another. Changes in polymer composition or structure that increase resistance to relative movement of the chains increase the strength and decrease the plasticity of the material. Substitutions into the backbone that increase its rigidity hinder movement of the chains. Bulky side groups also make disentanglement more difficult. Increasing macromolecule length (molecular weight) also makes the chains less mobile and hinders their relative movement.

Degradation of polymers requires disruption of their macromolecular structure and can occur by either alteration of the covalent interatomic bonds in the chains or alteration of the intermolecular interactions between chains. The former can occur by chain scission (cleavage of chains) or crosslinking (joining together of adjacent chains), and the latter can occur by incorporation (absorption) or loss (leaching) of low molecular weight compounds [6]. Polymers may contain various

additives, traces of catalysts, inhibitors, and other chemical compounds needed for their synthesis. Over time in the physiological environment, these compounds can leach from the polymer surface. As is the case with corrosion by-products released from metallic implants, the chemicals released from polymers may induce adverse local and systemic host reactions that cause clinical complications. In addition to unintensional degradation, certain polymers have been designed to undergo controlled degradation [4].

Biodegradable polymers may be useful as internal fixation device (i.e. screws) with an elastic modulus similar to bone. Approximately 100μm is the minimum pore size for effective bone ingrowths. Most synthetic porous implant materials in use have a random pore size of 100-500μm. A most remarkable property of calcium phosphate ceramics is their ability to bond directly to bone [7].

For several decades, body parts have been replaced or repaired by direct substitution of natural tissue or selected synthetic materials. In Table 2 is a list of polymeric materials in current clinical use is given. The majority of surface modifications for short-term blood compatibility are covalent or non-covalent immobilization of bioinert hydrophilic polymer chains onto the material surface. One of the hydrophilic polymers is polyethylene oxide (PEO) [8,9,10].

Table 2 Polymers in current clinical use [10].

POLYMER	**AREA OF USE**
Polyethylene (low density)	Reconstructive surgery
Polyethylene (UHMWPE)	Orthopaedics
Silicone Rubber	Plastic surgery, Orthopaedics
Polyacetal	Orthopaedics
Epoxy Resin (composite)	Orthopaedics
Polyesters	Cardiovascular
Polyamides	Sutures
Fluoropolymers	General surgery, Cardiovascular
Hydrogels	Ophthalmic, Retard drug

Table 2 (Continued)

Polyvinylchloride	Tubing
Polylactic acid	Sutures
Polyglycolic acid	Sutures
Rubber synthetic	Anaesthetics
Polymer of natural origin: Fibrin, Collagen, Gelatine, Dextran, Xanthan, Chitosan	Hemostatic agent, Absorbable implant, Sutures

Up to the present, various kinds of materials such as ceramics, metal and plastics have been used as artificial bone to fill bone defects or to replace bony structure. However, problems are still present as a material interfaces infection, loosening and fracture. To overcome these disadvantages, the ideal employing biodegradable materials, which may eventually be replaced by new-formed host bone tissue, seems to be interesting. Biodegradable artificial bone is under developing to be utilized only where high mechanical strength is not required, i.e. to replace cancellous bone with a biodegradable polymer such as polylactic acid and hydroxyapatite composites [11].

Flexible polymeric material capable of rapid and firm bonding with bone hydroxyapatite (HA) are required for orthopedic and oral surgery [12-13]. The pioneering research of Bonfield and his coworker has shown that several advantages could be obtained by combining bioactive ceramic with synthetic polymer such as polyethylene. This led to the development of bone-analogue composites, namely hydroxyapatite (HA) reinforced polyethylene [14]. The possibility of reinforcing new emerging biodegradable polymers as an alternative to polylactic acid has not been been fully explored yet [8].

1.2. Hydrogels

Hydrogels are hydrophilic natured three dimensional networks, held together by chemical or physical bonds. If enough instertitial space exists within the network, water molecules can become trapped and immobilized, filling the available free volume [15,16]. Figure 1 illustrates the hydrogel network [17].

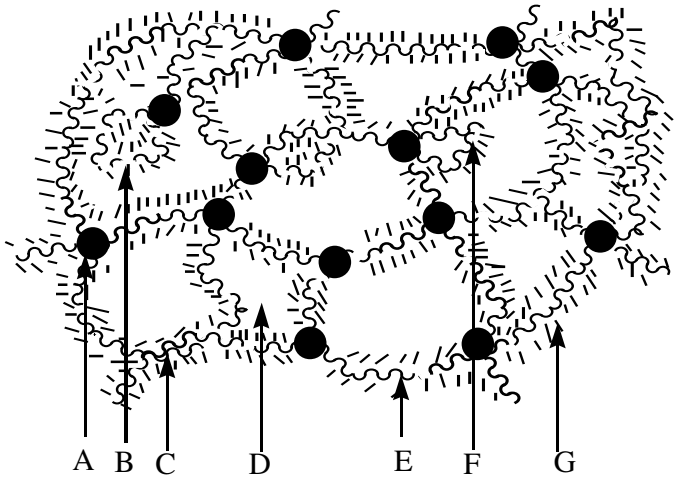


Figure 1 Hydrogel network. A: Interchain link, B: Loop 1, C: Entanglement D: Free water, E: Hydrophllic chain, F: Loop 2, G: Bound water.

The networks are composed of homopolymers or copolymers, and are insoluble due to the presence of chemical crosslinks (tie joints, junctions), or physical crosslinks, such as entanglements or crystallites [18,19]. The latter provide the network structure and physical integrity. These hydrogels exhibit a thermodynamic compatibility with water which allows them to swell in aqueous media [20,21,22].

Hydrogels can be classified as neutral or ionic, based on the nature of the side groups. According to their mechanical and structural characteristics, they can be classified as affine or phantom networks. Additionally, they can be homopolymer or copolymer networks, based on

the method of preparation. Finally, they can be classified based on the physical structure of the networks as amorphous, semicrystalline, hydrogen bonded structures, supermolecular structures and hydrocolloidal aggregates [19,20].

If hydrogel is dried, the swollen network of the hydrogel is collapsed during drying due to the high surface tension of water. Thus, the dried hydrogel (xerogel) becomes much smaller in size than the hydrogel swollen in water. During swelling and shrinking process, hydrogels can preserve its overall shape.

A hydrogel swells for the same reason that an analogous linear polymer dissolves in water to form an ordinary polymer solution. If a hydrogel dissolves in aqueous solvent, the gel has become a hydrosol, which is a dispersion of colloidal particles in water, simply speaking hydrosol is an aqueous solution. The polymer networks of small particles with diameter smaller than 1μm (≈ 100 nm) are called microgels. Microgels, however, dissolve in water like linear or branched macromolecules due to their molecular nature. The dried hydrogel is called a xerogel or dry gel. During the drying process water evaporates from the gel and surface tension causes the collapse of the gel body. If water removed without disturbing the polymer network, either by lyophilization (i.e. freeze drying) or by extraction with organic solvents, then the remaining material is extremely light with a Porosity as light as 98 percent. Such a dehydrated hydrogel is called an aerogel or sponge, not all dried hydrogels (xerogel) maintain the ability to swell in water [23, 24].

Hydrogels may show a swelling behaviour dependent on the external environment. These systems tend to show drastic changes in their swelling ratio as a result. Some of the factors affecting the swelling of hydrogels include pH, ionic strength, temperature and electromagnetic radiation [25]. Hydrogels exhibiting pH dependent swelling behaviour can be swollen from ionic networks. These ionic networks contain either acidic or basic pendant groups. In aqueous media of appropriate pH and ionic strength, the pendant groups can ionize, developing fixed charges on the gel. As a result of the electrostatic repulsions, the uptake of solvent in the

network is increased [26,27].

Temperature sensitive hydrogels can be classified as positive or negative temperature sensitive systems. A positive temperature sensitive hydrogel has an upper critical solution temperature (UCST). Such hydrogels contract upon cooling below the UCST (i.e. swelling at high temperature and shrinking at low temperature). Negative temperature sensitive hydrogels have a lower critical solution temperature (LCST). These hydrogels shrink as the temperature increases above the (LCST).

The chemical structure of the polymer may also affect the swelling ratio of the hydrogels. Hydrogels containing hydrophillic groups swell to a higher degree compaired to those containing hydrophobic groups because hydrophobic groups collapse in the presence of water, thus minimizing their exposure to the water molecule.

The crosslinking extent is one of the most important factors that affects the swelling of hydrogels. Highly crosslinked hydrogels have a tighter structure and will swell less compaired to the same hydrogels with lower crosslinking ratios. Crosslinking hinders the mobility of the polymer chain, hence lowering the swelling ratio [26].

Due to their high water content, hydrogels usually have low mechanical strength, although the research on hydrogels is more than three decades old, the research interest in hydrogel is still growing because the unique properties that have made the hydrogels find numerous applications in pharmaceutical, agricultural, and biomedical fields, Table 3 shows the monomers mostly used for pharmaceutical applications [27-28]. Hydrogels used in some important products are given in Table 4 [29].

Table 3 Monomers commonly used in synthetic hydrogels for pharmaceutical application [27-28].

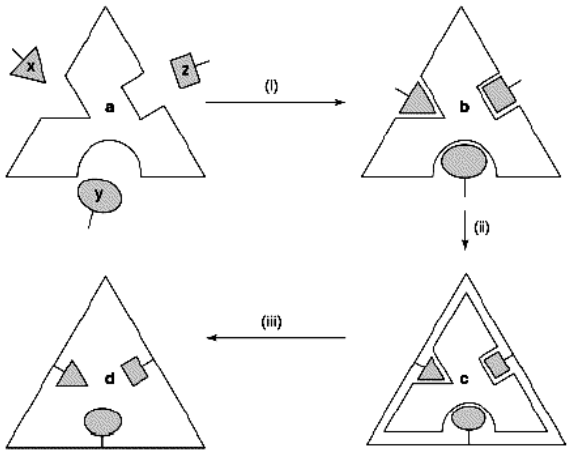
Monomer abbr.	Monomer	**Monomer abbr.**	Monomer
HEMA	Hydroxyethyl methacrylate	**Vac**	Vinyl acetate
HEEMA	Hydroxyethoxyethyl methacrylate	**AA**	Acrylic acid
HDEEMA	Hydroxydiethoxyethyl methacrylate	**MAA**	Methacrylic acid
EEMA	Ethoxyethyl methacrylate	**HPMA**	N- (2 hydroxypropyl) methacrylamide
MEEMA	Methoxyethoxyethyl methacrylate	**EG**	Ethylene glycol
EGDMA	Ethylene glycol dimethacrylate	**PEGMA**	PEG methacrylate
NVP	N-vinyl-2-pyrrolidone	**PEGDA**	PEG diacrylate

Table 4 Hydrogels usage in important products [29].

Hydrogel	**Use**
Crosslinked Gelatin	Photographic materials
Polyacrylamide gel	Electrophoretic media
Agarose gel	Cultivation media
Crosslinked polyacrylic acid	Super-absorbent gel
Crosslinked acrylic, methacrylic acid & vinylic hydrogel (as PHEMA)	Soft contact lenses
Crosslinked polyethylene oxide & polymethacrylic acid	Pharmaceuticals

1.3 . Template Polymerization

Template or matrix polymerization can be defined as a method of polymer synthesis in which specific interactions between preformed macromolecule (template) and a growing chain are utilized. Figure 2 illustrates the Template Polymerization [30]. These interactions affect the structure of the polymerization product (daughter polymer) and the kinetics of the process [31]. The term “template polymerization” usually refers to one phase systems in which monomer, template, and the reaction products are soluble in the same solvent.



(x, y, z) functionalized monomers

(i)	Complexation	(a) template molecule
(ii)	Polymerization	(b) pre-polymerization complex
(iii)	Template removal	(c) post-polymerization complex
		(d) polymer after template removal

Figure 2 Template Polymerization [30].

To study template systems it is important to compare the template process and products of the reaction with conventional polymerization

carried out under the same conditions. It is typical to replace template by a low molecular non-polymerizable analogue. The influences of the template on the process and the product are usually called “template effect” or “chain effect” [32].

The template effects can be expressed as:

1. kinetic effect; usually an enhancement of the reaction rate, change in kinetic equation.
2. molecular effect; influence on the molecular weight and molecular weight distribution. In the ideal case, the degree of polymerization of daughter polymer is the same as the degree of polymerization of the template used.
3. effect on tacticity; the daughter polymer can have the structure complementary to the structure of the template used.

The template processes can be realized as template polycondensation, polyaddition, ring opening polymerization, and ionic or radical polymerization [33].

1.3.1 Template Polycondensation

Template polycondensation or more generally speaking, template step polyreaction, is seemingly the most similar to natural synthesis of polypeptides or polynucleotides which occurs in living organisms. Two main types of polycondensation are well known in the case of conventional polycondensation. They are heteropolycondensation and homopoly-condensation. In the heteropolycondensation two different monomers take part in the reaction. In the case of homopolycondensation, one type of monomer molecule is present in the reacting system. The results published on the template heteropolycondensation indicate that monomer is incorporated into a structure of the matrix and then the second monomer can react with so activated molecules of the first monomer [34]. The mechanism can be represented as in Figure 3 [34].

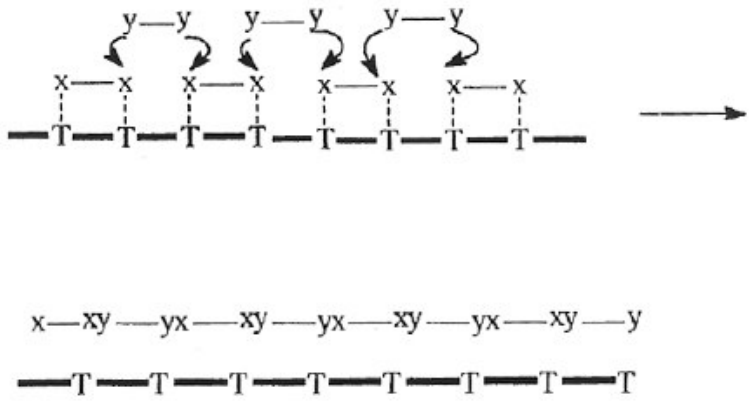


Figure 3 Template heteropolycondensation [34].

In this case one monomer with groups x can be adsorbed on the template –T-T. The second monomer with groups y reacts, forming a daughter polymer having groups xy and the template is available for further reaction. In another case of template heteropolycondensation two reagents with groups x and y can be adsorbed on the template. If groups in monomer molecule, which interact with the matrix, are not located at the ends of the molecule, we can imagine that ordering of monomer molecules on the template takes place according to the scheme given in Figure 4 [35]. The mechanism of template homopolycondensation can be represented in Figure 5 [35]. The monomer molecule has two different reacting groups x and y. One or both groups can interact with the template. In all cases of template heteropolycondensation, the reaction begins at a randomly selected point of template. Usually a simple linear macromolecule of template interacts from one side without creating a three dimensional growing center. It is very probable that some template irregularities complicate mechanism (Figure 6) [35].

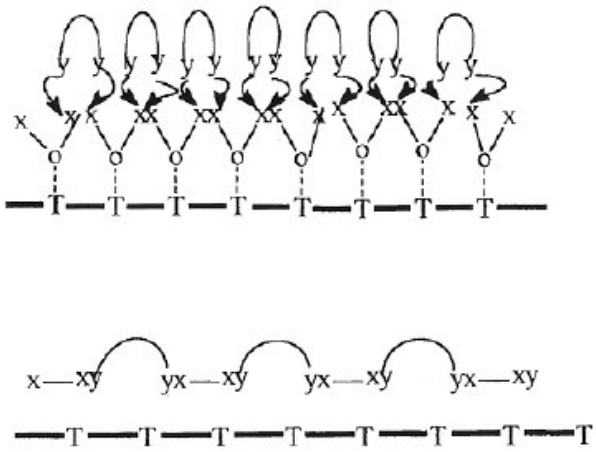


Figure 4 Mechanism of template polyheterocondensation in which groups located inside one monomer molecule interact with the template [35].

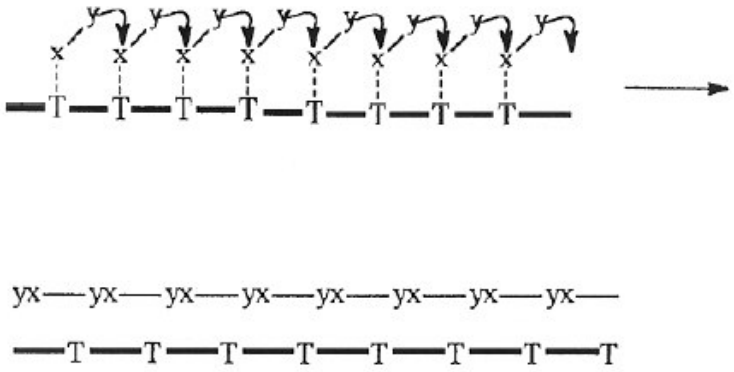


Figure 5 Template homopolycondensation [35].

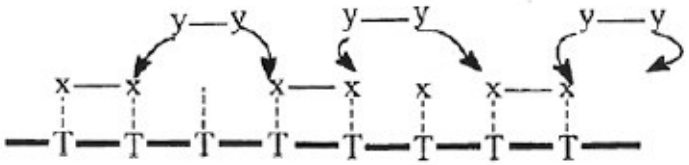


Figure 6 Irregular absorption onto the template [35].

1.3.2. Chain Template Polymerization

It is generally accepted that, for chain processes, there are at least three elementary processes: initiation, propagation and termination. Intermolecular forces lead to absorption of the monomer on the template or, if interaction between monomer and template is too weak, oligoradicals form complexes with the template. Taking into account these differences in interaction, this case of template polymerization can be divided into two types [36]. In type I, monomer is preadsorbed by, or complexed with, template macromolecules. Initiation, propagation and perhaps mostly termination take place on the template. The mechanism can be represented by the scheme given in Figure 7 [36].

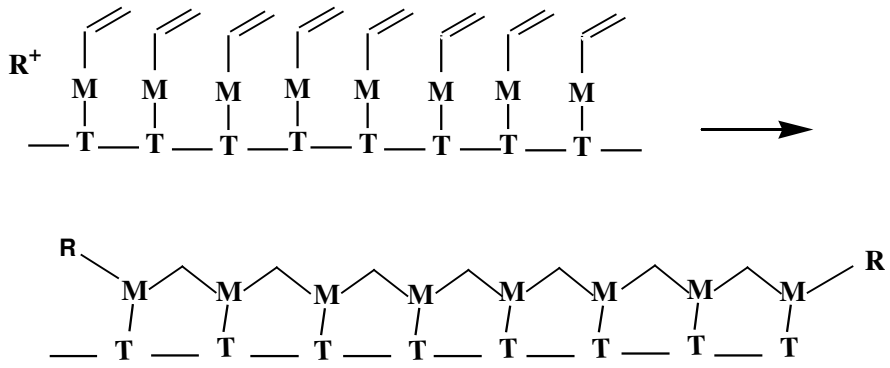


Figure 7 Chain template polymerization of Type I [36].

On the template unit, -T-, monomer, M, having double bounds is adsorbed. Radical, R•, initiates propagation process which proceeds along the template, and eventually a complex of the template and the daughter polymer, consisting M units, is created. In the extreme case of template polymerization, proceeding according to mechanism I, the monomer units are attached to the template by covalent bonding. The substrate of this reaction can be called multimonomer, the product after template

polymerization can be called as ladder type polymer. Chain template polymerization of multimonomer, very similar to Figure 7, is presented in Figure 8 [36]. The only difference between Figure 7 and 8 is that hydrogen bonding in Figure 7 is replaced by covalent bonding between T and M in Figure 8 in both the substrate and the product .

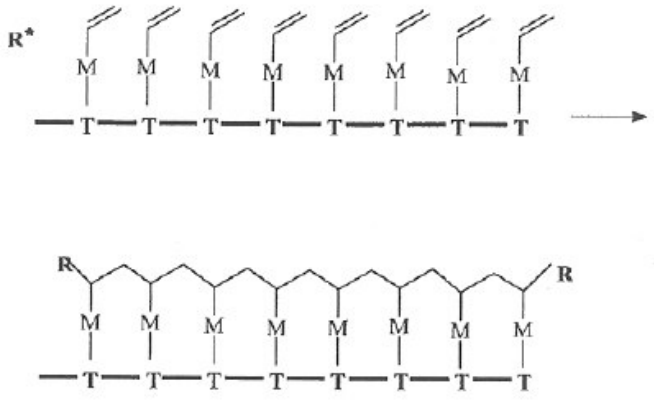


Figure 8 Chain polymerization of multimonomer [36].

In type II mechanism, the interaction between monomer and template is too weak to form a complex. Initiation begins in a free solution. When oligoradicals reach a proper length (critical chain length), their complexation occurs and then oligoradicals continue to propagate along the template by adding monomer molecules from the surrounding solution. The propagation process in the case of Type II template polymerization is shown in Figure 9 [36].

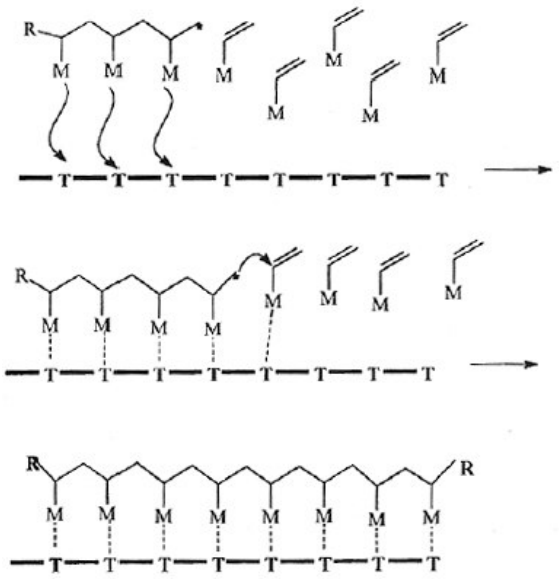


Figure 9 Chain template polymerization of Type II [36].

Termination can be realized both by macroradicals on the template (template - template termination) or by recombination of radicals on the template with macroradicals or oligoradicals not connected with the template (cross – termination). For some systems, it is difficult to decide whether they are type I or type II. The intermediate systems can also exist.

1.3.3. Template Copolymerization

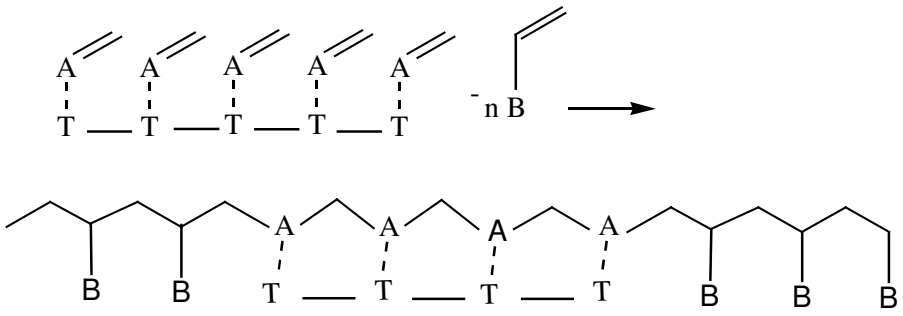
In template copolymerization, the interaction between comonomers and the template could prearrange monomer units defining sequence distribution in the macromolecular product. As in the case of template homopolymerization, template copolymerization can be realized according to different types of reaction: stepwise (template polycondensation), copolyaddition, ionic polymerization, ring opening copolymerization, etc.

Investigation of radical template copolymerization has been slightly more extensive. The classification of template copolymerization systems can be based on the type of interaction between the monomer and the template as was done for homopolymerization. Three basic types of such

interactions can be recognized: covalent bonding, strong intermolecular forces, and weak interactions between template and oligomers exceeding the critical length. However, these interactions can vary when two different types of comonomer are used. Possible cases of such reactions are presented in Figure 10 [37].

A

1)



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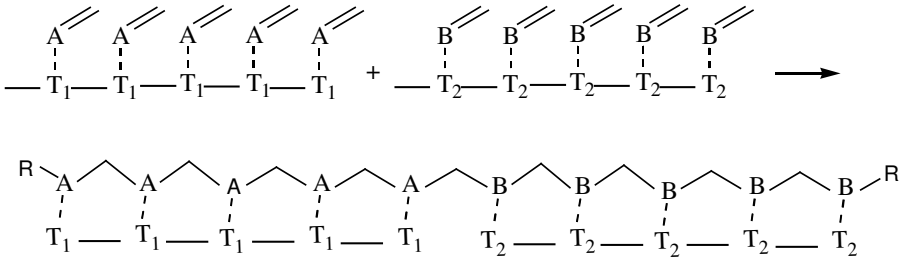

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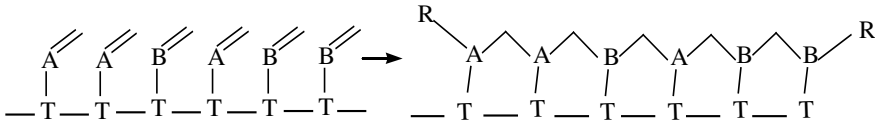
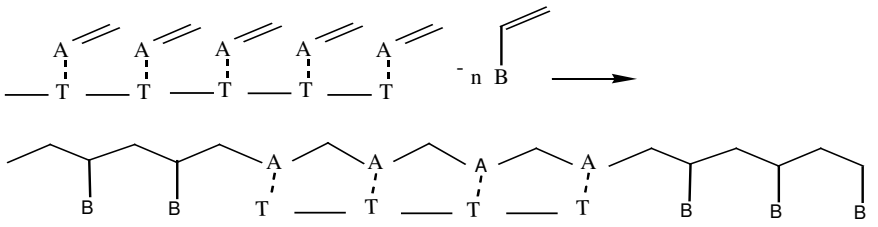


B

1)



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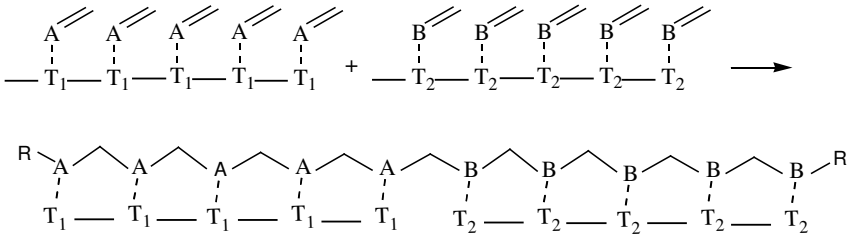

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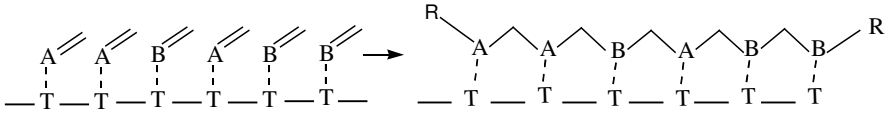

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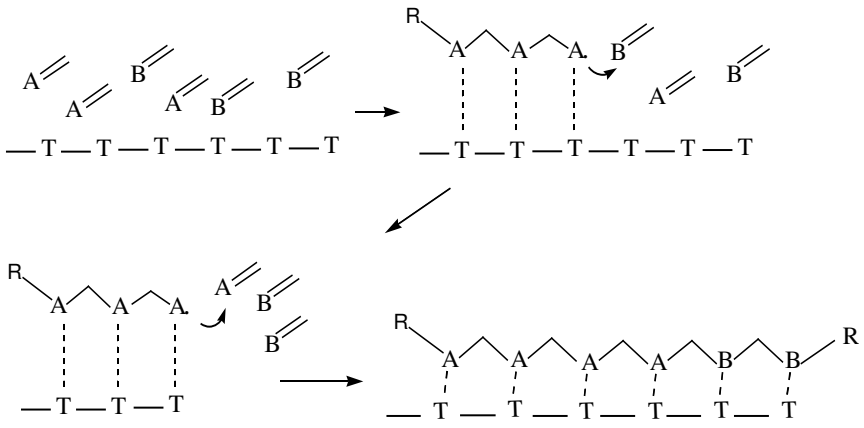


Figure 10 Schematic representation of template copolymerization [37].

Point A1 deals with the case in which at least one of the comonomers is connected with the template by covalent bonding. In particular: A1 represents the reaction of multimonomer with free monomer B (not connected to the template). One type of units A with double bonds is connected by covalent bonds to the template units,T. As a result of polymerization, a copolymer with ladder blocks is formed.

A2 shows the reaction between two different multimonomers. Two different type of units A and B, containing double bonds, are attached to two different templates. After polymerization, the ladder block copolymer can be formed. However, one can not exclude formation of a mixture consisting two unconnected ladder homopolymers.

A3 deals with polymerization of multimonomer in which two different types of groups are connected with one template by covalent bonding. In this case, two types of units A and B with double bonds are deposited onto one template. It is worth noticing that the order of units is controlled by process of synthesis of multimonomer, not by copolymerization process, as in conventional copolymerization. Point B deals with the case in which at least one of the comonomers interacts with the template due to strong intermolecular forces. In particular: B1 shows the reaction of one comonomer which is free why the second comonomer A is bound. B2

represents the reaction of two comonomers adsorbed onto two different templates, B3 shows the reaction of two comonomers connected with the same template.

Point C deals with the case in which interactions between both comonomers and the template are weak and complexation is possible with oligoradicals. One or both comonomers can interact weakly with the template. As was the case of Type II template homopolymerization, oligomeric radicals are adsorbed by the template and then propagation proceeds, at least partially, in close contact with the template [38].

1.3.4 Products of Template Polymerization

Two types of polymer materials can be obtained as a result of template polymerization:

1. polymers or copolymers with at least partially ladder type structure
2. polycomplexes with a structure of a more ordered form than obtained by mixing two polymer components.

1.3.4.1 Polymers With Ladder Type Structure

Zipping up reaction very seldom leads to polymers with full ladder structure. Very often the reaction proceeds with a break in the ladder, and isolated reactive groups are present in the product. If monomer units are connected by covalent bonds within the frame of the template and polymerization proceeds according to the “zip mechanism”, a product with ladder type structure can be expected. The structure of products obtained depends on the competition between the reactions proceeding on the template and the reaction between groups belonging to different macromolecules. Moreover, structure investigations are very difficult because ladder polymers are mostly insoluble [39]. NMR analysis by simple techniques is also impossible.

1.3.4.2 Polymers Complexes

Polymerization of monomers interacting with template by ionic or charge transfer interactions or by hydrogen bonding leads to polycomplexes. Formation of polymeric complexes from two mutually interacting polymers is well known [40]. By mixing two solutions of polyelectrolytes having opposite charges, one can obtain the polymeric complex usually in the form of precipitate or liquid phase containing a high concentration of the two polymeric components and a second liquid phase containing much lower concentration of the polymers. A structure of typical polycomplexes is illustrated in Figure 11a and 11b [41].

If one polymer has much higher molecular weight than the other, a model “host guest” is commonly applied (Figure 11a). Smaller “guest” molecules are absorbed on the “host” molecule. Because hydrophobic interactions take place between created blocks, the molecule of the complex becomes more compact. Similar intermolecular interactions can lead to precipitation. It seems probable that similar process takes place at the very beginning of the template polymerization proceeding according to “pick up” mechanism. The case in which two macromolecular components have high molecular weight is presented in Figure 11b. Interacting molecules are bonded at random. Short “ladder” parts of the polycomplex as well as “loops” created from unconnected parts of the components are present in the product. Such structure is sometimes called “ scrambled eggs” model.

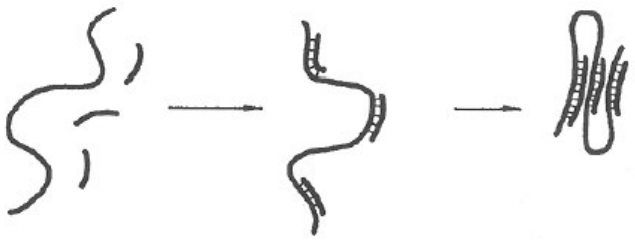


Figure 11a Polycomplex creation from high molecular weight polymer and oligomeric molecules [41].

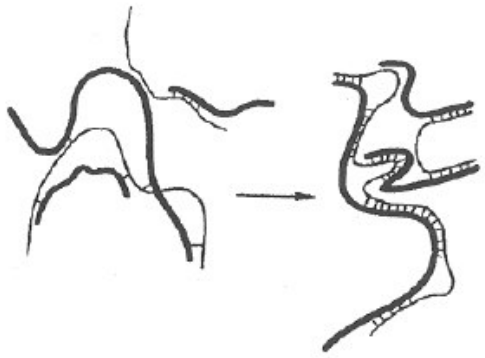


Figure 11b Polycomplex formation from two high molecular weight polymers. “Scrambled eggs” model [41].

1.4. Polymeric Foams

A polymeric foam is a dispersion of a gas in a polymeric material. The solid, cellular structure of the polymer is filled with one or more gases. The physical and mechanical properties are differ significantly from the unfoamed polymer. Foams can have excellent heat and sound insulation properties due to their high resistance against mass transport. Other foams have the ability to absorb a lot of energy, which makes them very useful in cushioning and packaging applications.

Another advantage of polymeric foams is the low amount of polymer mass needed to obtain the same volume as the unfoamed polymer. This is due to the introduction of the gases. A disadvantage is the relatively expensive production process and the fact that the knowledge about foams and foaming is mainly based on emprical observations [42].

An important property of polymer foams is their density. In general one can distinguish three different classes of foams, when considering their density [43]. High density foams have a density, which is between 500 kg\m^3 and 1000kg\m^3. Main applications of high density foam are in coaxial cables, due to their relative low dielectric constant in wood substitudes and in automotive applications. Medium density foams have a density between 100 kg\m^3 and 500kg\m^3. These foams are mainly used in packaging applications and in construction working. Low density foams

are with a density lower than 100 kg\m^3. In these foams tha ratio of the gas volume to polymer volume is equal to or larger than 10. Due to their low heat and sound conductivity these foams are mainly used in insulation applications.

Foaming processes are characterized by techniques that cause tiny bubbles to form within the plastic solidifies the bubbles, or at least the holes created by the bubbles, remain. The solidified bubble-containing material can be thought of as a cellular structure. Two types of cells occur in cellular plastics.

The first cell type is a closed cell structure (i.e. polystyrene), wherein each of the cells within the plastic is a separate, discrete entity. These closed cells can be compared to a tiny balloon or pockets. The walls have no holes in them. If the walls are appropriately impermeable, each cell can hold a gas.

The second cell type is an open cell structure (i.e. melamine), wherein the cells are interconnected (each cell is connected to other cells through holes in its wall). The cells cannot hold gas. Rather, gases move easlily within and throughout the entire cellular structure. This type of structure is like sponge. Plastic foams can also be classified on the basis of wall stiffness. If the walls are stiff, the foam is called a rigid foam. If the walls collapse when pressed, the foam is called a flexible foam. Both open and closed cell foams can have either flexible walls or rigid walls [44].

1.5. Aim of the study

The aim of this study is to produce a microporous structure hydrogel from methacrylic acid (MAA), vinyl pyrrolidone (VP) and polyethylene oxide (PEO). MAA-PEO-VP microporous polymer complex were characterized by its swelling, morphology, thermal, Porosity and spectroscopic properties.

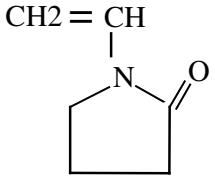
CHAPTER 2

EXPERIMENTAL

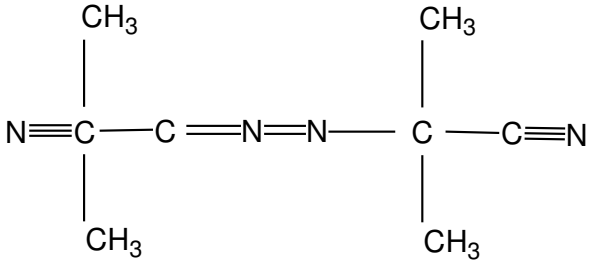
2.1. Materials

Polyethylene oxide powder [Aldrich, low molecular weight polyethylene oxide (LMPEO) M_v = 2 X 10^5] was used in this study.

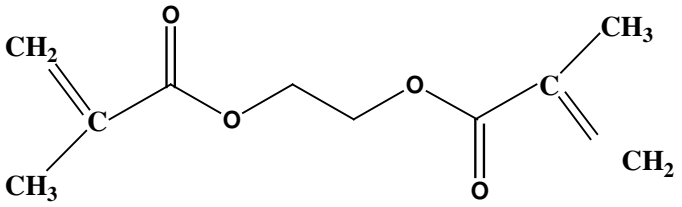
Methacrylic acid (MAA) which has a boiling point at 163ºC and Vinyl Pyrrolidone (VP) which has a boiling point at 92ºC were supplied from Aldrich. Tetrahydrofuran (THF), α,α'-Azoisobutyronitrile (AIBN) were the product of Merck, and Ethylene glycol dimethacrylate (EGDMA) was supplied from Fluka. They were used without further purification. The structures of the monomers, initiator and crosslinking agent used are shown below;

VP: 

, MAA: $CH_2=C(CH_3)-CO_2H$

AIBN: 

EGDMA:



2.2. Synthesis of porous structural material from MAA, VP & PEO

This thesis covered the synthesis of porous structural material from methacrylic acid and vinyl pyrrolidone monomers and polyethylene oxide polymer by using template polymerization. VP and MAA were dissolved in THF. And also PEO was dissolved in THF in another beaker. Both solutions were then thoroughly mixed, stirred and heated at nearly 45°C in a beaker with a mechanical stirrer for 1 hr (Figure 12). AIBN was then added to the mixture, after 1 h the viscous solution was cooled and EGDMA was added to the system. After a 1h period mixing, this viscous solution was transfered in separate test tubes. These test tubes were later heated in water bath at 50ºC ±1 for 3 h, Figure 13.

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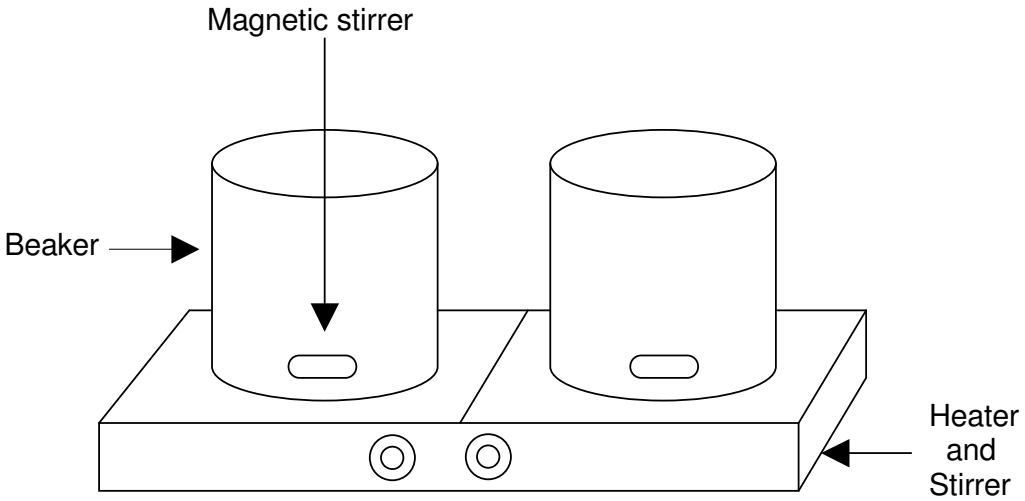

Figure 12 Experimental set-up of mixing of VP-MAA, and PEO.

The reaction ingredients and their weight percents are listed in Table 5. Two different microporous products with a homogeneous pore size distribution are obtained. The difference between them is their EGDMA weight percentages.

Table 5 Weight percentages of the reaction ingredients of two different VP-MAA-PEO hydrogels I and II in 10ml THF.

Ingredients	VP	MAA	PEO	AIBN	EGDMA
Weight (g)	11.2	8.6	1	0.05	0.05
Weight (g)	11.2	8.6	1	0.05	0.10

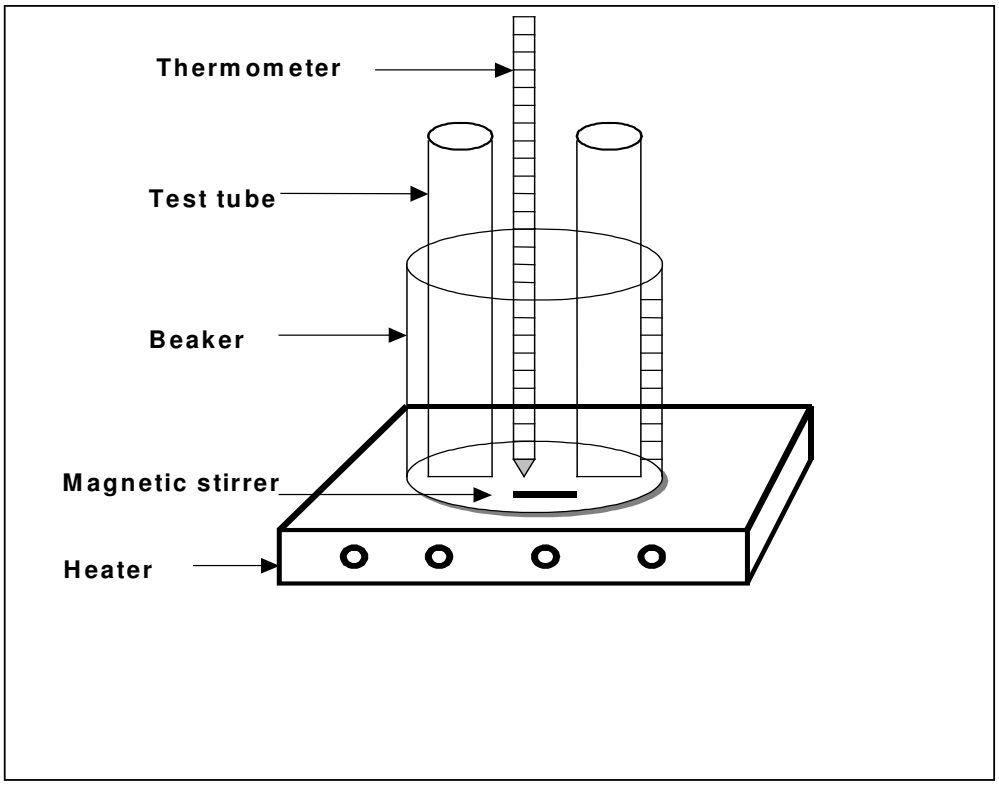

Figure 13 Experimental set up of microporous VP-MAA-PEO complex formation [45].

2.3. Characterization

2.3.1. Equilibrium Swelling Ratio.

The equilibrium degree of swelling (ES) of two polymers having different crosslinking ratios were determined in deionised water at different temperatures (20°C, 30°C, 35°C, 37°C, 40°C). Cylindrical small pieces of VP-MAA-PEO samples (r = 11.5mm, h = 3mm) were equilibrated in distilled water up to 6h, and samples then removed from water; confined with filter paper in 10 seconds then weighted immediately. The equilibrium degree of swelling was calculated according to the following equation:

$$E\,S = \left(\frac{\text{wt. of swollen sample - wt. of dry sample}}{\text{wt.of dry sample}} \right) \times 100$$

Equilibrium degree of swelling of microporous VP-MAA-PEO complexes of the same size were also carried out in different solutions: pH 1.0, pH 4.5, pH 7.2, pH.9, pH 11 which were adjusted by 0.2N HCl and 0.2N NaOH at two different temperatures (20°C and 37°C). ES was then calculated as mentioned above.

2.3.2. Scanning Electron Microscopy (SEM)

Morphological studies were carried out on tensile fractured surfaces of two kinds of VP-MAA-PEO samples at various magnifications, after gold plating by using scanning electron microscope, JEOL, JSM-6400.

2.3.3. Differential Scanning Calorimetric Analysis (DSC)

Thermal properties of two kinds of VP-MAA-PEO complex polymers were analyzed in TA instrument of DSC 910 S. Heating rate was adjusted at 20°C/min, the temperature range was between -25°C and 250°C and sample size was varied between 8-11 mg.

2.3.4. Spectroscopic Measurements

FTIR spectra of two kinds of VP-MAA-PEO complex polymers were examined by using Nicolet DX-5 FTIR spectrometer.

2.3.5. Porosity Measurements

Porosity of VP-MAA-PEO complex polymers were examined by using Quantachrome Autosorb Automated Gas Sorption System.

CHAPTER 3

RESULTS AND DISCUSSION

3.1. Preparation of Crosslinked Microporous VP-MAA-PEO Hydrogels

In this study, VP-MAA-PEO hydrogels were prepared by template polymerization of MAA and VP monomers in the presence of PEO with molecular weight of $2x10^5$. Two different kinds of hydrogels were synthesized. The only difference between them was their crosslinking ratios. All were prepared by dissolving MAA and VP monomers and PEO in THF, separately. The polymerization was carried out with AIBN as an initiator at 50ºC for nearly 24 hours. For this system EGDMA was used as crosslinking agent.

The characterization of hydrogels were done by Infrared Spectrometry (IR), Scanning Electron Microscopy (SEM), Differential Scanning Calorimetry (DSC), Porosity measurements and also Equilibrium Swelling Tests which were done at different pH values and different temperatures. And finally, the results of these two hydrogels were compared to each other.

3.2. Equilibrium Swelling Ratio of Hydrogels Prepared

The equilibrium swelling ratio of VP-MAA-PEO hydrogels were determined at different pH values and at different temperatures.

First, the determination of swelling behaviour of the hydrogels were characterized in water over a temperature range from 20ºC to 40ºC. Dried hydrogel disks dimensions of 3x11.5 mm were immersed in water at 20ºC, 30ºC, 35ºC, 37ºC and 40ºC and water swelling was measured as a

function of time. Figure 14 presents the ES values of LXL VP-MAA-PEO hydrogel .

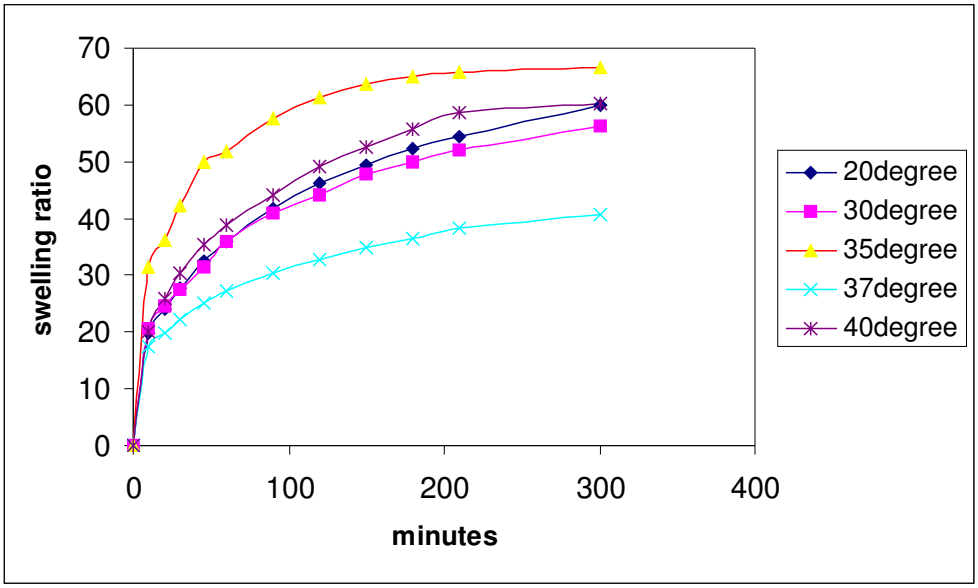

Figure 14 ES values of LXL VP-MAA-PEO hydrogel characterized in water over a temperature range of 20ºC - 40ºC

The ES ratio showed a maximum value at 35ºC and minimum value at 37ºC. However, the ES values did not show a regular change with temperature. For example the ES ratio was bigger at 20ºC than that of 30ºC and also 37ºC.Figure 15 represents the ES values of HXL VP-MAA-PEO hydrogel.

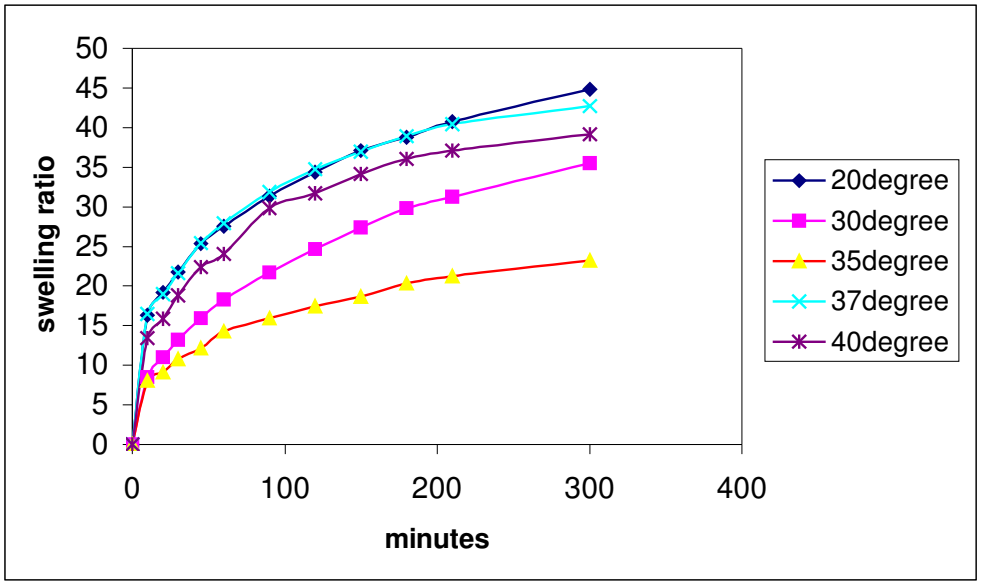

Figure 15 ES values of HXL VP-MAA-PEO hydrogel characterized in water over a temperature range of 20ºC - 40ºC

The ES ratio had maximum at 20ºC and minimum at 35ºC, unlike the ES ratio of the LXL sample. The ES ratio values of the first hydrogel were obtained bigger at each temperature values than that of the second hydrogel. Because highly crosslinked hydrogels had a tighter structure, had lower mobility of the polymer chains hence lower swelling ratio.

Secondly, the swelling behaviour of these hydrogels were characterized over a pH range from 1 to 11. The weight of each dried VP-MAA-PEO hydrogel disks was measured before the swelling experiment. These disks were immersed in solutions made from 0.2N NaOH and 0.2N HCl and with pH range of 1-11 at 25ºC and 37ºC, separately.

Figure 16 shows the swelling ratios of LXL VP-MAA-PEO hydrogel at different pH values and at 25ºC.

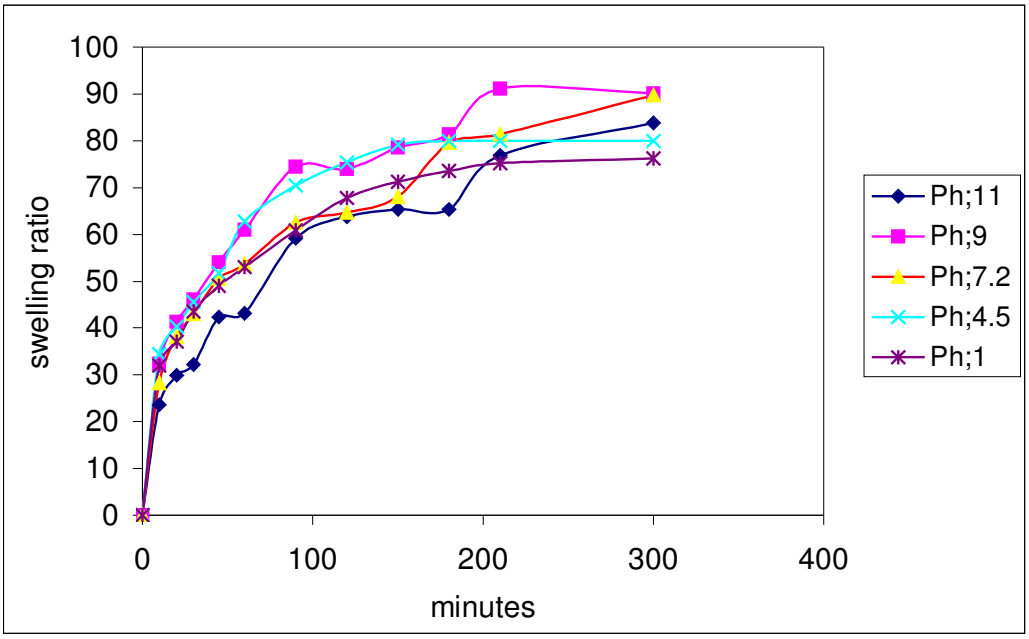

Figure 16 ES of LXL VP-MAA-PEO hydrogel at different pH values and at 25ºC.

The swelling mostly occured at pH;9,0. The swelling ratio decreases with decreasing pH values. Although, there was an exceptional case pH;11. At pH;11 the ES ratio was small. The swelling is almost independent of pH within the experimental error limits. The swelling approaches a platue value around 80 at all pH values. The effect of pH on the swelling behaviour of the HXL hydrogel at 25ºC was found to be distinctly different as given in Figure 17.

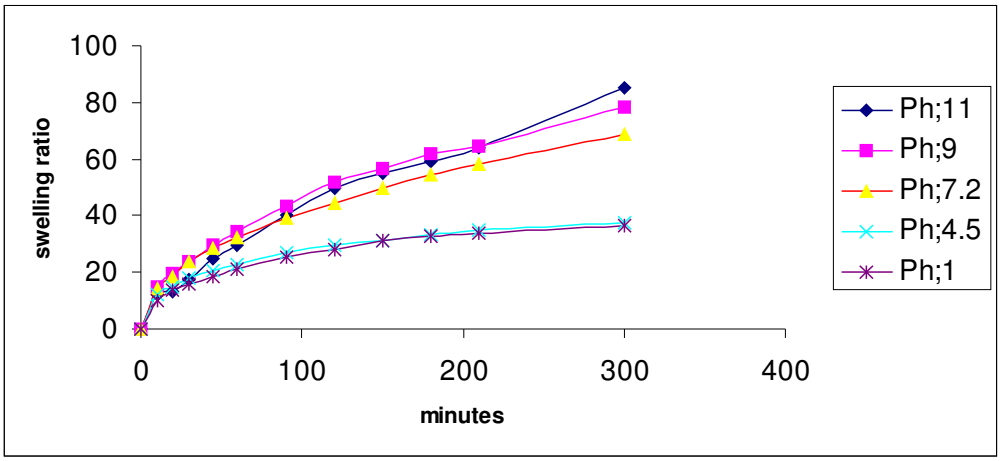

Figure 17 ES of HXL VP-MAA-PEO hydrogel at different pH values and at 25ºC.

At pH's lower than 7.2, the swelling did not reach even 50 while above pH;7.2 (just even at 7.5). The swelling ratio increased upto 80. It seems strongly that HXL showed pH dependent behaviour compared to LXL at the same temperature. The HXL one had smaller ES ratio than that of LXL one as we obtained from the first part of the experiment, due to the same reasons. Figure 18 represents the behaviour of LXL VP-MAA-PEO hydrogel at 37℃ with different pH values.

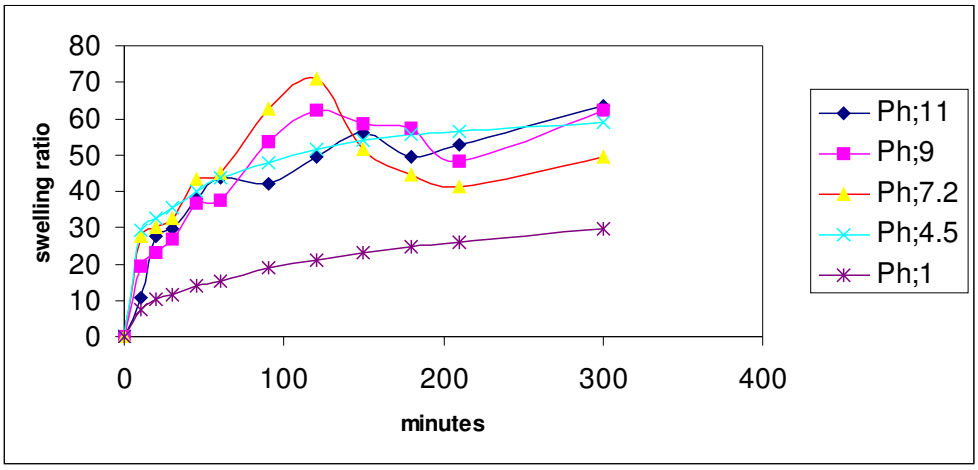

Figure 18 ES of LXL VP-MAA-PEO hydrogel at different pH values and at 37ºC.

This graph is nearly the same as Figure 16, however, the swelling values are smaller than that of Figure 16. The swelling ratio of this hydrogel had its maximum values at pH 9 and 11 and when pH was 1 the swelling ratio had its minimum value.

Figure 19 shows the comparison of different pH values which respect to time of HXL VP-MAA-PEO hydrogel at 37ºC.

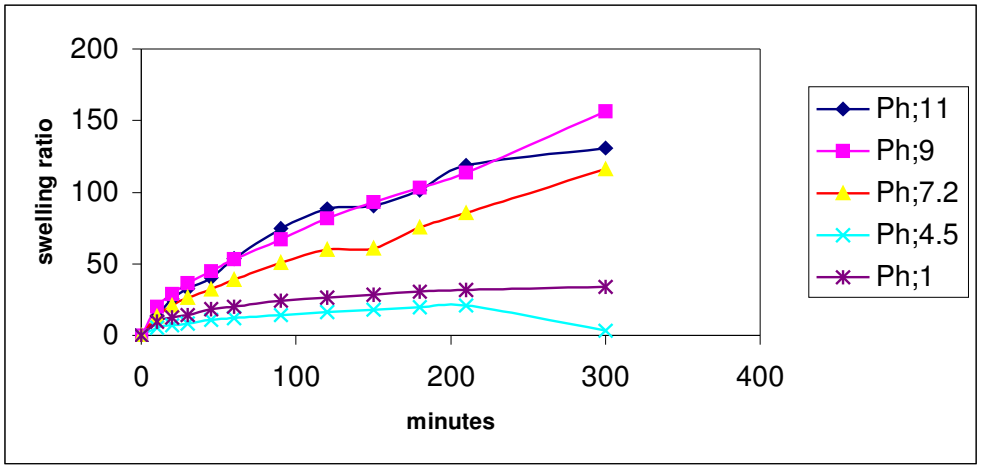

Figure 19 ES of HXL VP-MAA-PEO hydrogel at different pH values and at 37ºC.

Like other graphs, the swelling ratio of this hydrogel had its maximum value at pH;9 and minimum value at pH;4.5.

From all these graphs it can easly be seen that the swelling values of LXL VP-MAA-PEO hydrogel at 25ºC are bigger than that of HXL one, and at 37ºC they are smaller than that of HXL hydrogel. Hydrogels which shows pH dependent swelling behaviour like our samples can be swollen from ionic networks, which contain acidic or basic pendant groups. In aqueous media of different pH the pendant groups can ionize, developing fixed charges on the gel. As a result of the electrostatic repulsions, the uptake of solvent in the hydrogel is increased, because of the increasing hydrophilicity of the hydrogel.

In our case, hence our hydrogel is acrylic based hydrogel, it showed relatively small swelling ratios in low pH solutions and extremely high degrees at high pH regions. And also carboxylic acid groups on the hydrogel backbone were converted to the protonated acid from when the hydration was carried out in a solution of pH < 4.5. A low swelling ratio indicated that the water content for the acid form of the hydrogel was low.

When the solution pH was above 7.2, the carboxylic acid groups were converted to the salt form and the maximum degree of swelling was achieved. And when these two kinds of hydrogels were compared, the same results were obtained as the first part of the swelling experiment results, “crosslinking hinders the mobility of the polymer chain, hence lowers the swelling ratio”.

3.3. Scanning Electron Microscopy (SEM)

In order to examine the relationship between the morphological structure and the template surface of hydrogel, SEM was performed.

Figure 20 shows the fracture surface of HXL and LXL crosslinking agents including polycomplexes at different magnifications. The main differences between these figures at a first look are, particle size distributions and the number of cavities in structures.

As can be seen from Figure (a) and Figure (b), there is more disperse distribution leading less number of cavities and smaller sized particles in HXL structure than that of LXL one.

We see tortuous pathways in HXL structure and smooth pathways in LXL structure at magnifications of X5000 (Figure (c), (d)) and X10000. It is more clear to see these properties at magnification of X10000, in Figure 20 (e) and (f). This result is parallel to dispersion behaviours of these two systems, more homogeneous distribution in HXL one.

In addition to these, there existed more free spaces in LXL structure and LXL is less rigid and softer than that of HXL one, according to these SEM photos.

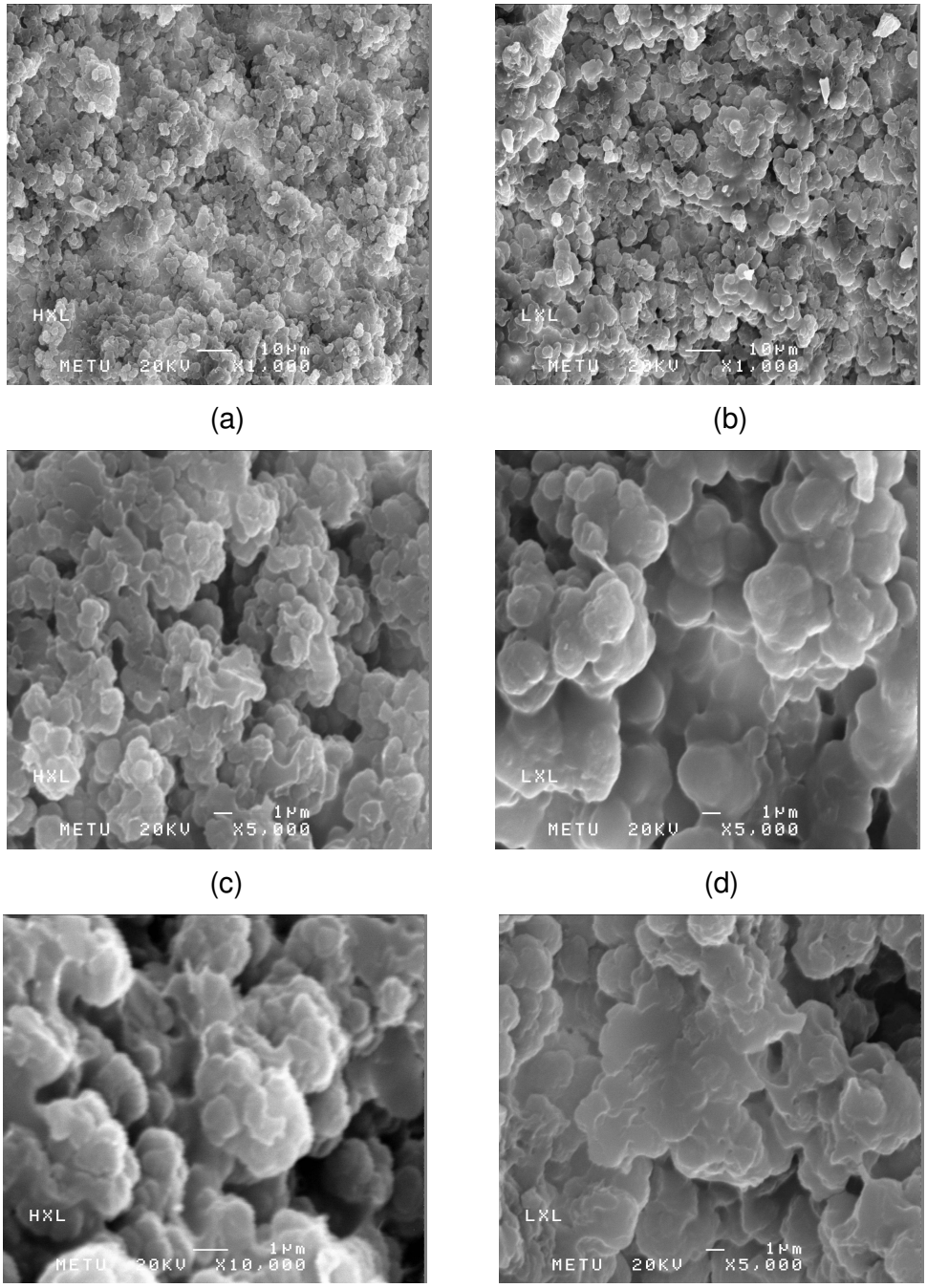

Figure 20 SEM pictures of HXL and LXL hydrogels at different magnifications.

3.4. Differential Scanning Calorimetry Analysis

In order to understand the thermal behaviour of VP-MAA-PEO hydrogel, thermal analysis were carried out, and also these thermograms were compared with that of pure PEO.

PEO which is a highly crystalline polymer shows its melting point at 69ºC. Figure 21 presented in the DSC thermogram of PEO. [45]

PMAA which shows a good thermal stability until about 180ºC has a Tg at 135ºC and PVP stable over a wide range of temperature to degrade at about 380ºC has its Tg at 158ºC.[46]

The DSC thermogram of LXL VP-MAA-PEO hydrogel has two distinct thermal transitions, at about 59.71ºC and 127.23ºC. Figure 22(a) shows the DSC thermogram of LXL hydrogel and 22(b) shows the derivative of this thermogram.

The first transition corresponds to the melting temperature of PEO, and the second corresponds to the MAA and VP template polycomplex, a secondary transition, possibly a glass transition.

Figure 23(a) illustrates the thermal behaviour of HXL hydrogel. This graph has nearly the similar properties with the former one. The first transition is at 60.32ºC and the second corresponding is at 124.78ºC. The derivative reveals the same behaviour (Figure 23(b)).

It was expected that the thermal transitions of HXL hydrogel had to be higher than those of LXL one. This was mainly because of the increase in intermolecular interactions caused by increasing the level of crosslinking. Addition of crosslinking agent to the medium, unfortunately did not caused the radical change in melting temperature values.

In conclusion, crosslinking apparently did not alter the thermal transition temperatures so much and therefore PEO seems to crystallize alone. On the other hand the peak height of crystalline melting point of PEO was apparently very small because of presence of these two other monomers acting as daughter polymer of PEO. PMAA and PVP polymerization in the matrix showed only a single glass transition at around 124-127ºC which was lower than that of PVP (Tg: 158ºC) and

lower than that of PMAA (Tg: 135ºC). However, the other secondary transition of PMAA and PVP at lower temperatures 68 - 36ºC, respectively were not seen at DSC thermograms.

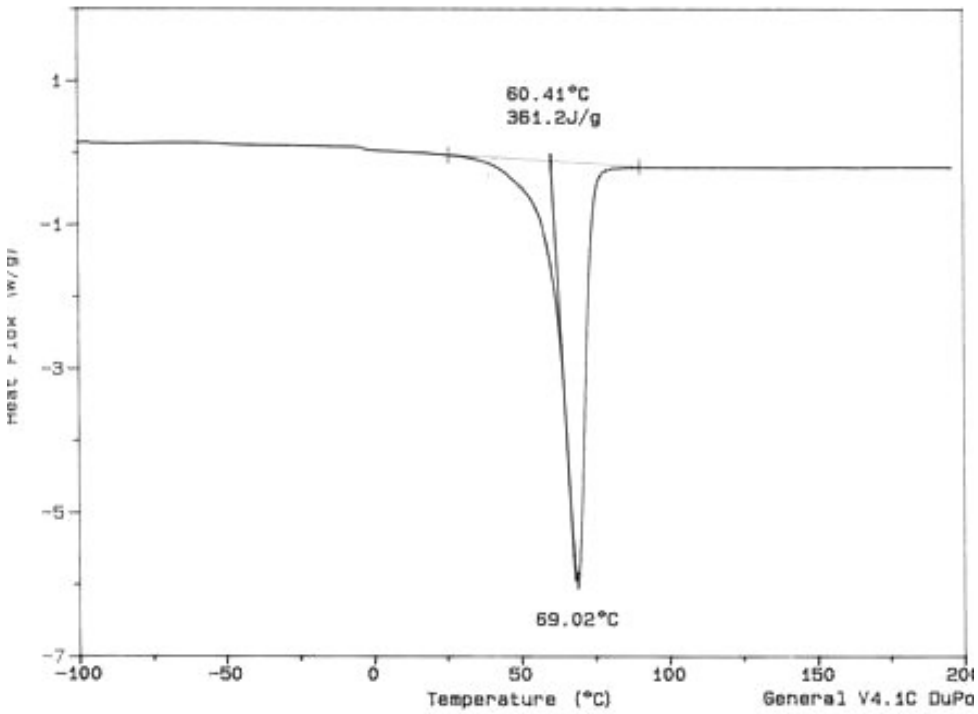

Figure 21 DSC thermogram of pure polyethylene oxide

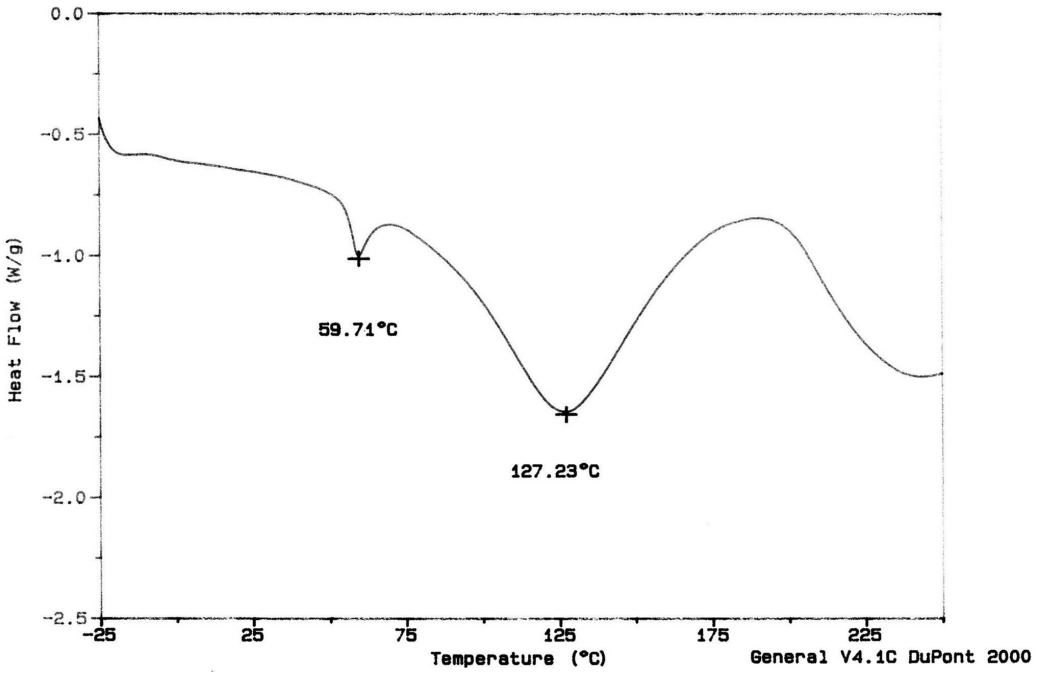

Figure 22 (a) DSC thermogram of LXL hydrogel

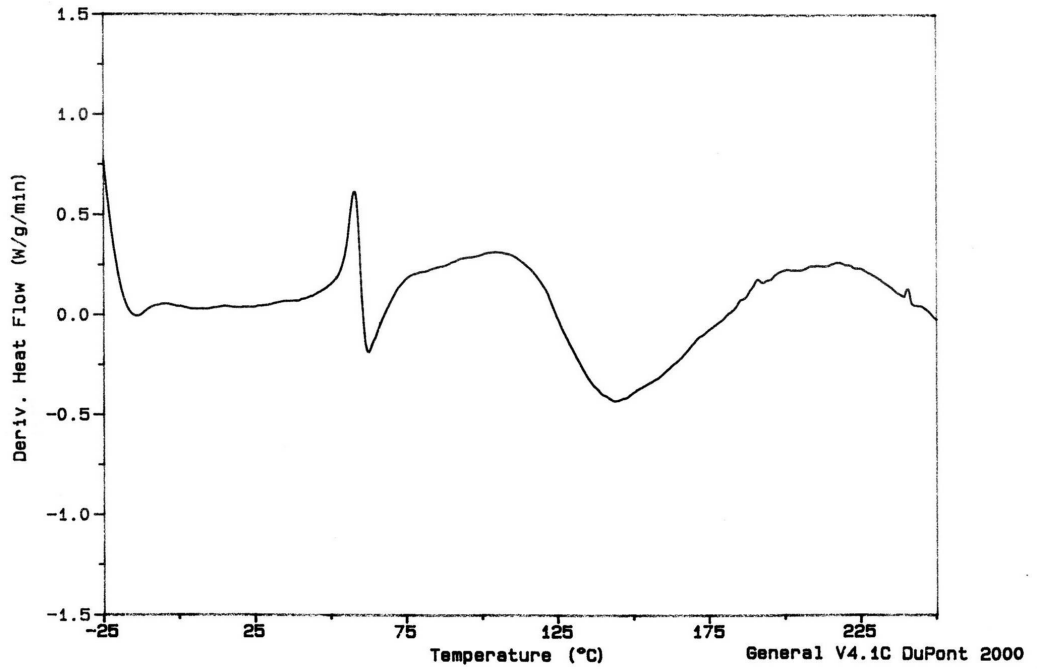

Figure 22 (b) Derivative thermogram of LXL hydrogel

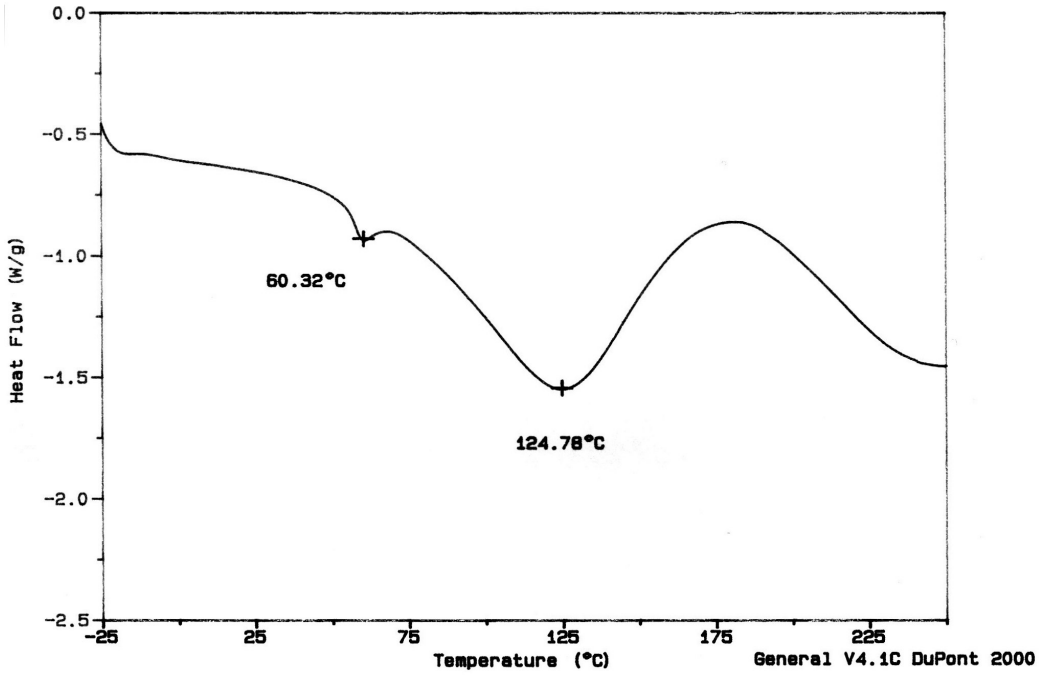

Figure 23 (a) DSC thermogram of HXL hydrogel

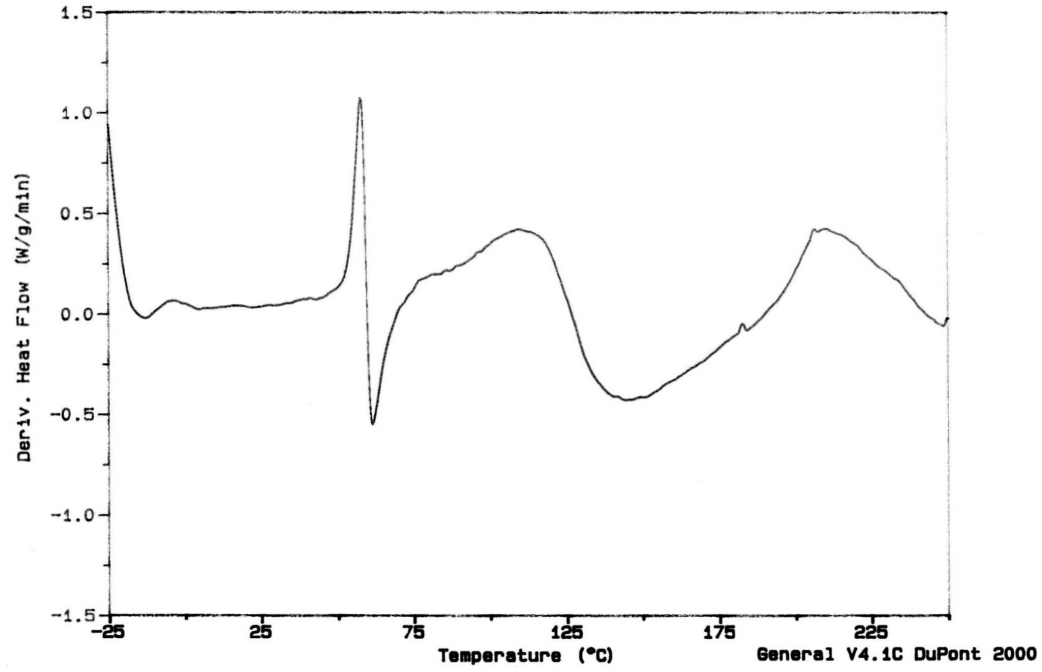

Figure 23 (b) Derivative thermogram of HXL hydrogel

3.5. Spectroscopic Measurement Analysis

From the template polymerization of MAA-VP initiated by AIBN in THF in the presence of PEO, a white insoluble powdery product was obtained. The IR spectrum of this product having LXL ratio and HXL ratio were shown in Figure 24, Figure 25, respectively.

These spectra are qualitatively identical. In both spectra, there is band $\nu_{c=0}$ = 1666 which had a shoulder at 1725cm^{-1} corresponding to an ester, is due to the C=O vibrations of acids showing internal hydrogen bonding [47]. Free OH stretching frequency for polymeric association (3400 – 3200 cm^{-1}), C-OH in plane band 1390 cm^{-1}, C-O stretching (1169 cm^{-1}), C-N stretching (1450 cm^{-1}) and C-O-C band absorption of PEO (1050 cm^{-1}) are other important IR bands observed.

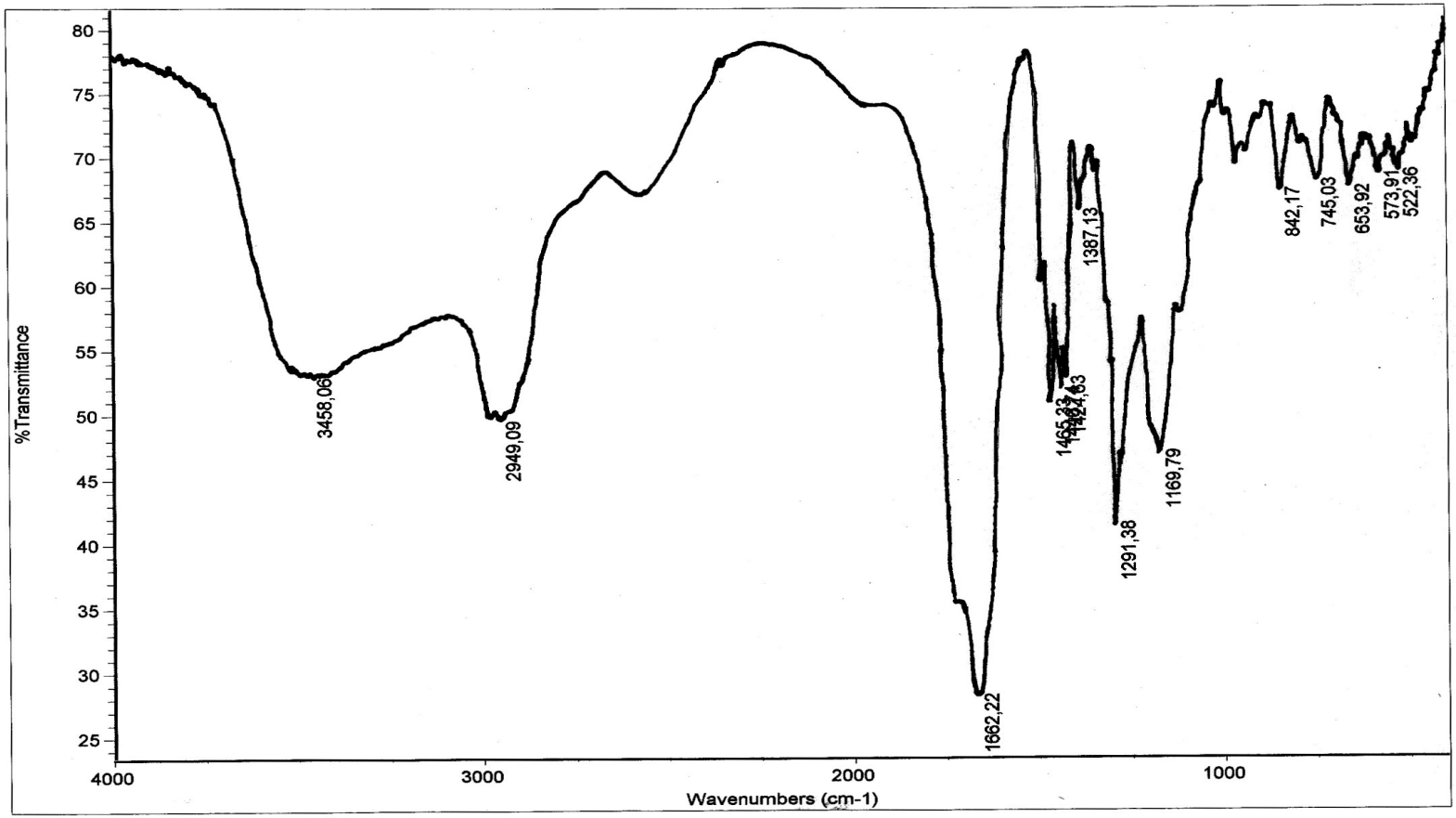

Figure 24 FTIR graph of LXL hydrogel

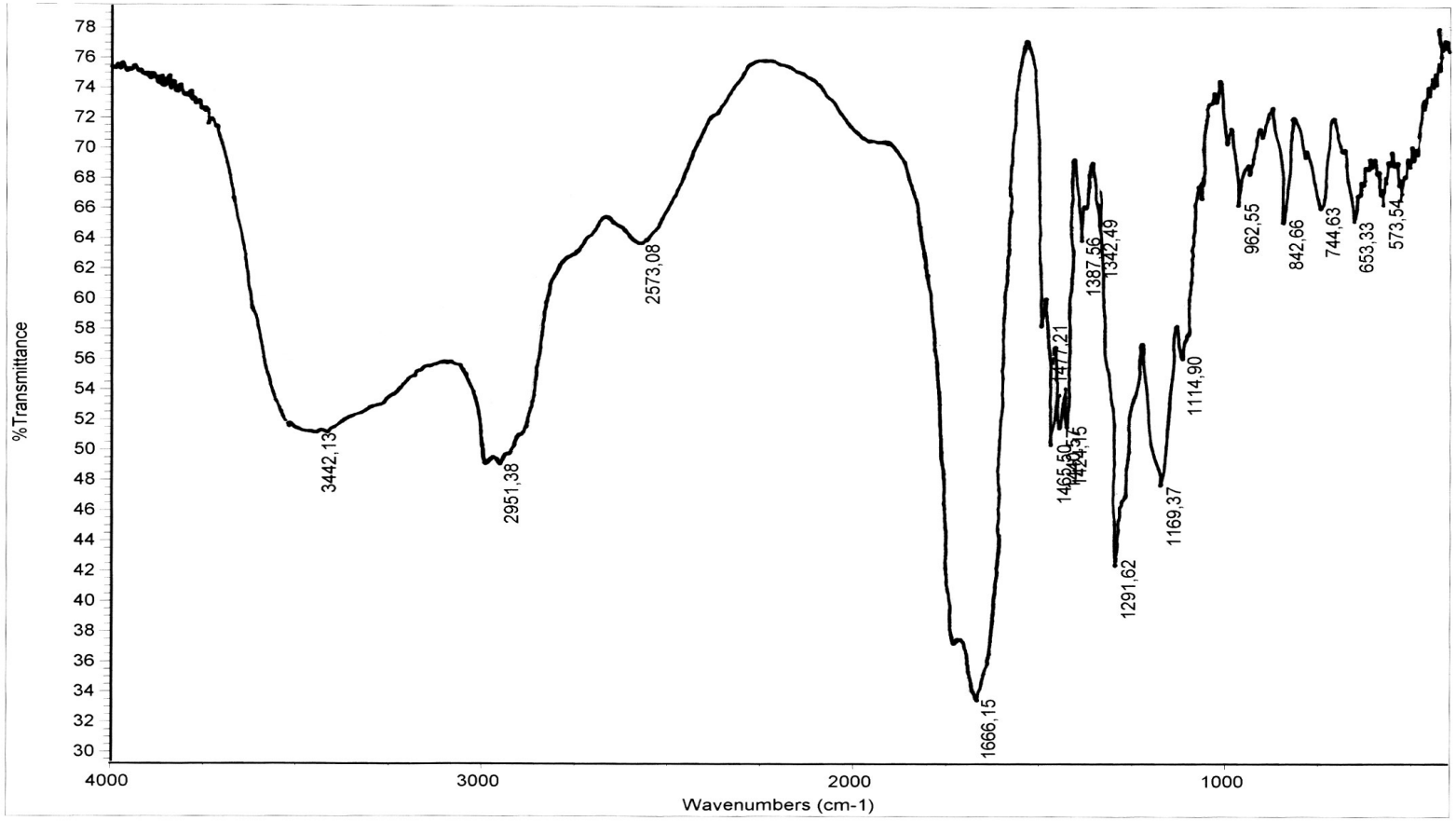

Figure 25 FTIR graph of HXL hydrogel

3.6. Porosity Measurements

Pore size of the hydrogel prepared was determined by using mercury intrusion porosimetry. Mercury intrusion and extrusion volumes were plotted vs. pore diameter on x-y coordinates. The specific surface area calculated was 2,34m^2/g. The slope was 1,004×10^3 and the intercept was 4,833×10^2. This histogram showed three peaks, the mean diameter observed around nearly 1100nm. The pore diameters can be seen from the histogram below (Figure 26). The large peak indicates that most of the pores existed in that size range, and the wider peaks indicate that the relatively larger segment of pore is followed by smaller ones.

Report date: 12/27/2004 Merged File

Quantachrome Instruments
Quantachrome Poremaster for Windows® Data Report
Version 4.03

Sample ID	PET-OH	**File Name**	S4C2401H_Merged.PRM
Sample Weight	0.5000 grams	**Bulk Sample Volume**	1.0000 cc
Sample Description	T. Tincer		
Comments	LP STATION 1		
Hg Surface Tension	480.00 erg/cm²	**Hg Contact Angle**	(I)140.00°,(E)140.00°
Minimum Delta Vol.	0.000 % FS	**Moving Point Avg.**	11 (Scan Mode)
Operator	K. Behlulgil	Mercury volume normalized by sample weight.	

Norm. Intr. Volume vs. Pore Size Histogram

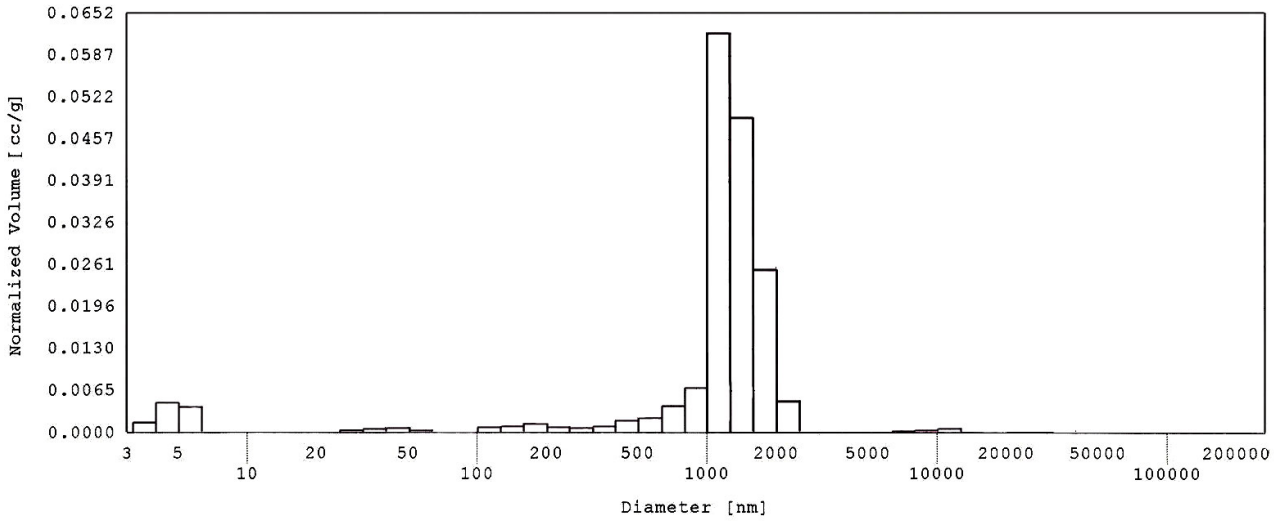

Figure 26 Pore size histogram for VP-MAA-PEO Hydrogel

CHAPTER 4

CONCLUSIONS

Two kinds of VP-MAA-PEO hydrogels which had different crosslinking ratios were synthesized and characterized.

The swelling tests done at different temperatures in water showed that HXL hydrogel had lower swelling ratios than that of LXL hydrogel. Because crosslinking hinders the mobility of the chain and lowers the swelling ratio. The ES values did not show a regular change with temperature. And the swelling tests done at different pH values either at 25ºC or 37ºC showed pH dependent swelling. pH;9 was the maximum value and pH;1 was the minimum value for LXL hydrogel at both temperatures. pH;11 was the maximum and pH;1 was the minimum for HXL hydrogel at 25ºC. pH;9 was the maximum and pH;4.5 was the minimum for HXL at 37ºC. These results were due to the carboxylic acid groups on the polymer backbone which were converted to the salt form when ph was bigger than 7.2 causing an increase in the swelling ratio and also because of the acrylic based properties showing swelling ratios in low pH solutions.

The morphological studies showed that HXL one had smaller sized particles which were homogeneously distributed than that of LXL one. On the other hand, LXL one had more free spaces and give softer touching.

The thermal behaviours of these two hydrogels were nearly the same like their spectroscopic properties determined by IR. In DSC thermograms the first transition corresponding to PEO was at 59.71ºC for LXL one and 60.32ºC for HXL one. The second transition corresponding to

VP-MAA polymer complex was at 127.23ºC for LXL one and 124.78ºC for HXL one. The difference between these values was because of the crosslinking agent amount increasing the intermolecular interactions.

In conclusion, these two hydrogels can be used for pharmaceutical applications, for example in drug release studies. Some work can be done for improving the properties of our polymer complex system.

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