SYNTHESIS AND CHARACTERIZATION OF MACROPOROUS POLY (DIMETHYLAMINO ETHYL METHACRYLATE) HYDROGELS BY ENHANCED PHASE SEPARATION

ARTTIRILMIŞ FAZ AYRILMASIYLA MAKROGÖZENEKLİ POLİ (DİMETİLAMİNO ETİLMETAKRİLAT) HİDROJELLERİNİN HAZIRLANMASI VE KARAKTERİZASYONU

OSMAN AGUŞ

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Osman Aguş

ABSTRACT

In this study, radiation synthesis and characterization of poly (N, N- dimethylamino ethyl methcrylate hydrogels by enhanced phase separation technique have been investigated.

Initial monomer mixtures containing various composition of N, N dimethylamino ethyl methacrylate (DMAEMA), water and ethylene glycol dimethylacrylate (EGDMA) and phase separator sodium chloride (NaCl), or poly (ethylene glycol) (PEG) have been prepared and irradiated in ^{60}Co gamma sources at 4 kGy. The effect of cross-linking agent, (EGDMA), sodium chloride and poly(ethylene glycol) content on the total percentage gelation were determined. Percentage gelation values of the prepared hydrogels were found by gravimetrically. FTIR spectra of gels were taken to explain the chemical structure of network.

For the characterization of network structure firstly, the uniaxial compression was applied using the Universal Testing Instrument on the swollen gels at pH 7. Stress-strain curves of poly(dimethylamino ethyl methacrylate) P(DMAEMA), hydrogels prepared in the presence of NaCl and PEG were evaluated to calculate Shear modulus values and molecular weight between the cross-links in the gel structure.

The molecular weight between cross-links of P(DMAEMA) hydrogels decreased with increasing amount of EGDMA, from 0.05% to 1.0% and increasing concentration of NaCl in the initial mixture from 1M to 3M. The molecular weight between cross-links of P(DMAEMA) hydrogels prepared in the presence of PEG increased with increasing amount of PEG in the initial mixture from 1% to 20%.

One of the important parameters characterizing the hydrogel systems is the mesh size. The mesh size characterizes the space between macromolecular chains. In this thesis, the network mesh size, ξ, was calculated by using the swelling data and polymer based constants. The mesh size in P(DMAEMA) hydrogels decreased from 22.6 to 6.4 nm with increasing cross-linking agent content in the hydrogel structure from 0.05 to 1.0 %. The mesh size in P(DMAEMA) hydrogels decreased from 10.9 to

3.4 nm with increasing NaCl content in the initial mixture from 1M to 3M. However, addition of PEG in the initial mixture decreased the crosslink density and increased the mesh size. The highest mesh size hydrogels have been obtained by using 20% PEG containing PEG10000.

For the investigation of the effect of pH on the swelling of P(DMAEMA) hydrogels, swelling experiments were followed at pH 3-8. The results showed that Equilibrium Degree of Swelling (EDS) values increased with decreasing of the pH due to cationic of the gels and decreased with increasing of cross-linking density of hydrogel system. In all PEG used systems maximum extent of swelling was reached at pH 3, this being due to protonization of amine groups of PDMAEMA at pH 3.

Effect of molecular weight of PEG on the swelling behaviour was investigated. It was found that with the addition of PEG, Equilibrium Degree of Swelling (Q) increases with increasing molecular weight of PEG until 10000 molecular weight. Over the 10000 molecular weight, the equilibrium degree of swelling didn't change or slightly decreased. Although, maximum extent of swelling was reached at 10000 molecular weight containing %1 and 5 % PEG.

Finally, Porous structures of hydrogels were examined using a scanning electron microscope (SEM). Analysis of the SEM micrographs showed that pore structures of hydrogels were very homogeneous and pores were opened with the decrease of pH, as expected.

Key Words: Hydrogel, gama irradiation, microphorous, pH sensitive, porogen

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ÖZET

Bu çalışmada poly(N,N-dimetilamino etil metakrilat) hydrogellerinin arttırılmış faz ayrılması tekniği kullanılarak radyasyonla sentezi ve ağ yapısının karakterizasyonu incelenmiştir.

Çeşitli bileşimlerde N,N-dimetilamino etil metakrilat(DMAEMA), su, EGDMA ve faz ayırıcı NaCl veya poli(etilen glikol) (PEG) içeren başlangıç karışımları hazırlanmış ve bunlar ^{60}Co gama kaynağında 4 kGy ışınlanmıştır. Çapraz bağlayıcı EGDMA nın, sodyum klorürün ve poli(etilen glikol) ün karışımların yüzde jelleşmesine olan etkisi belirlenmiştir. Sentezlenen jellerin yüzde jelleşme değerleri gravimetrik olarak tayin edilmiştir. Jellerin FTIR spektrumları ağ yapısının kimyasını açıklamak amacıyla alınmıştır.

Ağ yapısının karakterizasyonu için önce pH 7 de şişmiş olan jellere Universal test cihazı kullanılarak sıkıştırma testi uygulanmıştır. Sodyum klorür ve PEG varlığında hazırlanan P(DMAEMA) hidrojellerinin gerilim-uzama eğrileri modulus değerinin ve çapraz bağlar arasındaki molekül ağırlığının bulunması için değerlendirilmiştir.

P(DMAEMA) hidrojellerinin çapraz bağlar arasındaki molekül ağırlığı çapraz bağlayıcı madde miktarının % 0.05 den % 1.0 değerine ve sodyum klorür miktarının 1M dan 3 M arttırılması ile azalmıştır. PEG varlığında hazırlanmış P(DMAEMA) hidrojellerinin çapraz bağlar arasındaki molekül ağırlığı başlangıç karışımındaki PEG miktarının %1 den % 20 ye artması ile artmıştır.

Hidrojellerin ağ yapısının karakterizasyonundaki en önemli parametrelerden bir tanesi de gözenek büyüklüğüdür. Gözenek büyüklüğü makromolekül zincirleri arasındaki boşluğu karakterize eder. Bu çalışmada, gözenek büyüklüğü, ξ şişme verileri ve polimer bazlı sabitler kullanılarak hesaplanmıştır. P(DMAEMA) hidrojellerinin gözenek boyutu, çapraz bağlayıcı madde miktarının %0.05 den %1 e arttırılmasıyla 22.6 nm den 6.4 nm ye düşmüştür. P(DMAEMA) hidrojellerinin gözenek boyutu sodyum klorür konsantrasyonunun 1M dan 3M a çıkmasıyla, 10.9 nm den 3.4 nm ye düşmüştür. Ancak başlangıç karışımına PEG eklenmesi ile çapraz bağ yoğunluğu

düşmüş ve gözenek boyutu artmıştır. En yüksek gözenek boyutuna sahip hidrojeller %20 oranında 10000 molekül ağırlığında PEG içeren hidrojel sisteminde elde edilmiştir.

pH ın hidrojellerin şişme davranışına olan etkisinin incelenmesi için pH 3-8 aralığında şişme davranışları incelenmiştir. Sonuçlar, denge şişme değerlerinin (EDS) pH değerinin azalmasıyla arttığını ve çapraz bağlayıcı içeriğinin artışıyla azaldığını göstermiştir. PEG kullanılarak hazırlanan tüm sistemlerde en yüksek şişme pH 3 te olmuştur, bunun nedeni bu pH değerinde PDMAEMA yapısındaki amin gruplarının protonlanmasıdır.

Poli(etilen glikol) un molekül ağırlığının şişme üzerine etkisi incelenmiştir. Poli(etilen glikol) un molekül ağırlığının 10000 e kadar artmasıyla denge şişme değerlerinin de arttığı görülmüştür. 10000 molekül ağırlığının üzerine çıkmasıyla denge şişme değerleri değişmemiş veya bir miktar düşüş göstermiştir. Maksimum şişme değerlerine %1 ve %5 oranında, 10000 molekül ağırlığında poli(etilen glikol) kullanılarak hazırlanan sistemlerde ulaşılmıştır.

Son olarak, hidrojellerin gözenek yapıları elektron mikroskobu ile incelenmiştir. Elektron mikroskobu analizleri, hidrojellerin gözenek yapılarının homojen olduğunu ve pH ın azalmasıyla birlikte gözeneklerin açıldığını göstermiştir.

Anahtar Kelimeler: Hidrojel, gama ışığı, mikroporlar, pH duyarlı, porojen

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1. INTRODUCTION

Polymers are the compounds that are formed by contribution of different or identical groups having long chains and high molecular weight. Copolymers can be prepared by using two different monomers. They can be linear, branched or cross-linked. As cross-linked polymers, in the form of network, they are not soluble in any solvent and start to swell when they are in appropriate solvent after a certain time.

The term cross-linked polymer tends to be used for polymers where the individual chains may be distinguished and where the cross-links are short relative to the chain segments between the cross-links. Such structures may be formed either by cross-linking of preformed linear polymers, or during chain polymerization where a proportion of multifunctional monomers such as divinylbenzene and the diacrylates were used.

There are many ways of cross-linking of preformed linear polymers. In many cases a readily cross-linkable group is deliberately incorporated into the polymer to facilitate cross-linking, as in the important cases of the sulphur vulcanization of rubbers and the cross-linking of unsaturated polyesters through linking the unsaturated groups via chain polymerization of styrene. If free radicals can be generated on polymer chains then these may combine to produce cross-links. Several methods can be used for this purpose. e.g. heating with peroxides as in the peroxide vulcanization of rubbers, irradiating with high energy radiation (radiation cross-linking) or ultraviolet and visible light (photocross-linking).

Xerogel is the name given for the homo or copolymers with network or cross-linked structure that is able to imbibe solvent and then swell. When water is used instead of other solvents and if the xerogel has the ability to store more than twenty percent water of its mass then the xerogel is named as hydrogel.

A hydrogel can be considered as a container of water made of a three dimensional mesh. Many materials, both naturally occurring and synthetic, fit the definition of hydrogels. Dextrans, starch, alginates, and collagens are examples of natural polymers that can be cross-linked to form hydrogels. Hydrogels based on synthetic polymers include poly (hydroxyl alkyl methacrylates), poly (acrylamide), poly (ethylene oxide), poly (N-vinyl 2-pyrrolidone) and poly (vinyl alcohol). Wichterle and Lim (1960) were the first to suggest that a hydrogel based on poly (2-hydroxy

ethyl methacrylate) could be a synthetic biocompatible material.

Super absorbent polymer hydrogels are lightly cross-linked hydrophilic polymers that can absorb, swell and retain aqueous solutions up to hundreds of times of their own weight. These materials, firstly originated in the United States as water retention agents in agriculture, were developed in Japan in the mid 1970s in the personal care and hygienic products (disposable diapers, sanitary napkins, surgical pads, etc.) (Buchhlz F.L., and Graham T., 1998).

In addition to the healthcare products, they are used in soil conditioning and as artificial soils for hydroponics, controlled release agents for agrochemicals or pharmaceuticals, artificial snow for skiing areas. The other numerous properties desired for the features of super absorbents are

(a) High swelling capacity,

(b) High swelling rate, and

(c) Good strength of the swollen gel.

Conventional hydrogels have very low swelling capacity and rate. They mainly need several hours to reach the maximum absorption capacity. Majority of reported super absorbents comprise only the first feature mentioned, i.e. high absorbency, whereas they must also comprise high rate of swelling especially in certain applications, e.g. in the absorbents incorporated in the baby napkins. A kind of superabsorbent polymer named superporous hydrogel has developed in recent years by Chen and Park (Chen J., et al., 1999, 2000) for controlled delivery of drugs. Other researchers have recently extended the hydrogels for designing other drug delivery systems (Dorkoosh F. A., et al., 2000, 2001). So, creation of porosity in hydrogels is very important in many of applications.

Macroporous hydrogels find application as biocompatible implants in tissues, such as in the central nervous system (Woerley, S., et al, 1993 and 1999) or as substrates in cellular and tissue engineering (Oxley, H., et al 1993)

Porosity in hydrogels is usually achieved by one of four basic methods:

1- By cross-linking polymerization in the presence of substances that are solvents for the monomers, but precipitants for the formed polymer (Woerly S., et al 1993 and 1999, Oxley et al 1993).

2- By cross-linking polymerization in the presence of substances (sugar, salt) which can be washed out from the hydrogel after polymerization. This technique is called as enhanced phase separation technique (Oxley et al 1993)
3- By cross-linking polymerization in the presence of substances liberating gases which remain in the resulting hydrogel (Park K. and Park H. 1998)
4- By frost sublimation of the hydrogel swollen in water (Kato N. et al.,1997 and Shapiro L. et al., 1997)

By using any of these procedures, hydrogels with communicating or non-communicating pores can be obtained, i.e. the pores are or not interconnected.

The aim of this study is the preparation of macroporous DMAEMA hydrogels by enhanced phase separation via NaCl and PEG and investigation of the effect of NaCl and PEG content on the swelling behaviour and network properties of these hydrogels.

2. HYDROGELS

Recently hydrogels have found a wide range of biomedical applications including controlled drug delivery systems, replacement of blood vessels, wound dressing, soft tissue substitution, contact lenses and a variety of other related and potential uses. Hydrogels are generally found to be very well tolerated when implanted in vivo and can be easily tailored to suit the many functions of prosthetics in contact with blood or tissues. The success of hydrogels as biomaterials lies in their resemblance to living tissue because of their relatively high water content which minimizes the frictional irritation of surrounding tissue. Additional advantages of hydrogels are their non-toxicity, non-antigenicity, non-irritability, and chemical stability. The relatively high water content of hydrogels made them also permeable to small molecules like oxygen, nutrients, and metabolites. The high solute permeability of hydrogels made them ideal materials of choice as devices for the controlled release of drugs and other active agents. Much of the research on hydrogels has been focused on the application in controlled drug delivery. By proper design of hydrogels it is possible to control the kinetics of delivery of active ingredients.

Hydrogels form a specific class of polymeric biomaterials. Precise definition of this term is not obvious. Many years ago Dorothy Jordan Lloyd stated that "the colloidal condition, the gel, is one which is easier to recognize than to define" (Jordan-Lloyd D., 1926). Since that time more accurate definitions have appeared. Nowadays, hydrogels are defined as two- or multicomponent systems consisting of a three-dimensional network of polymer chains and water that fills the space between macromolecules. Depending on the properties of the polymer (polymers) used, as well as on the nature and density of the network joints, such structures in an equilibrium can contain various amounts of water; typically in the swollen state the mass fraction of water in a hydrogel is much higher than the mass fraction of polymer. Two general classes of hydrogels can be defined - physical gels (pseudo gels), where the chains are connected by electrostatic forces, hydrogen bonds, hydrophobic interactions or chain entanglements (such gels are non-permanent and usually they can be converted to polymer solutions by heating) and chemical (true, permanent) hydrogels with covalent bonds linking the chains. In this paper we deal with the formation and applications of permanent polymer networks.

According to the definition formulated above, hydrogels must be able to hold, in equilibrium, certain amount of water. This implies that the polymers used in these materials must have at least moderate hydrophilic character. In practice, to achieve high degrees of swelling, it is common to use synthetic polymers that are water-soluble when in non-cross-linked form. Typical simple materials applied for general-purpose hydrogels are poly (ethylene oxide)(Savaş H. and Güven O., 2001, and 2002), poly(vinyl alcohol)(Wu, M., et al., 2001), poly (vinyl pyrolidone)(Rosiak,J. M. and Yoshii, F., 1999) and poly(hydroxyl ethyl methacrylate)(Young, C.-D., et al, 1998). Some other polymers used for gels of special properties are stimuli-sensitive hydrogels. One should mention that although majority of hydrogels for biomedical purposes are made of synthetic polymers, there is also a number of examples where cross-linked natural polymers, mainly polysaccharides, are applied.

Although hydrogels have a number of non-biomedical applications (e.g. in agriculture), it seems that their use in the field of medicine and pharmacy is the most successful and promising (Rosiak J. M. and Yoshii F., 1999). Over 30 years of research in this field resulted in the common use of hydrogels as soft contact lenses, wound dressings, drug-delivery systems, superabsorbents etc. with a number of products being commercially available.

A part of this success can be related to the fact that some important properties of hydrogels, e.g. the ability to absorb aqueous solutions without loosing shape and mechanical strength, are commonly met in many natural constituents of a human body, like muscles, tendons, cartilage etc. Besides that, hydrogels usually exhibit good biocompatibility in the contact with blood, body fluids and tissues.

Nowadays a new class of hydrogels, capable of reacting to various environmental stimuli as temperature, pH, ionic strength, solute concentration, electric field, light, sound etc., is tested for use in the so-called "intelligent biomaterials" (Kaetsu I., et al, 1992, Hirasa O., 1993,).

The effect of some of these external stimuli on the hydrogel properties are explained below.

2.1. pH sensitive hydrogels

During the last couple decades many different kind of polymeric systems were proposed as drug carrier systems. One of these systems was poly-electrolyte polymers which contain relatively ionizable groups at level ranging from a few mol to 100% of the repeating units (Karadağ et al., 1995a, Saraydın et al 1995a, Güven et al., 1999, Şen et al., 1999)

Hydrogels undergo controllable change in response to small variation in solution conditions such as temperature, pH, and electric signal which are also employed the solution variables in typical physiological, biological and chemical systems (Tanaka T.,1987, Siegel R. A., and Firestone B. A., 1988, Kudela V., 1987, Kaetsu I., 1993, 1995, Kaetsu I., et al 1999).

The sensitivity of poly-electrolyte hydrogels on pH at a certain interval makes this system suitable for changes in the pH of the skin. The pH sensitivity also imparts additional advantages to these systems by causing an overall retardation in the release of drug as compared with non-electrolyte gels.

Yoshida et al. (1999) synthesized the thermo and pH responsive acryloyl-L-proline ether ester (A-ProOet) copolymers with methacryloyl-glycine (MA-Gly) and methacrylic acid as a novel biofunctional gel for application in colon delivery systems. The release of 2-(3-benzoylphenyl) propionic acid(ketoprofen) was studied in different buffer solutions. It was found that the copolymeric gel obtained by introducing 60 mol% MA-Gly or MA-Ac, the gel adopted a collapsed state at pH 3.0 for A-ProOet/MA-Gly gel and pH 5.5 for A-ProOet/MAAc gel and release of ketoprofen from these copolymer gels is closely related to swelling of the gels in response to pH changes. The cumulative amount of ketoprofen released from A-ProOet/Ma-Gly copolymer reached 100% in 1,5 h after start of the experiment in pH 7.5 buffer solution and 4h after in pH 5.5 buffer solution . However, at pH 3 the cumulative amount of released drug was only 14% even after 6 h had passed due to gel shrinkage. They also observed a correlation between gel swelling and drug release due to changes in pH of the medium.

Nakamae et al, (1996) synthesized phosphate group containing metacryloyloxethyl dihydrogen phosphate/N-isopropyl acrylamide copolymeric hydrogels for the delivery of positively charged enzymes. They investigated the influence of negatively charged phosphate group content in the gel on the positively charged

lysozyme enzyme uptake capacity of hydrogel and pH of the medium on the release properties of network structure. It was found that negatively charged phosphate groups bind ionically to positively charged lysozyme. It was also observed that the ratio of phosphate groups per one lysozyme molecule is 18, which is apparently equal to the number of positive charges on lysozyme. Increasing pH from 1.4 to 7.4 increased the degree of ionization of anionic polymer thus increased the enzyme release rate from gel system. They also recommended that this type of pH sensitive hydrogels should be ideal for delivering drugs to the small intestines, while avoiding release in the stomach.

2.2. Temperature sensitive hydrogels

Environmentally sensitive materials can also respond to the surrounding temperature. Hydrogels that can respond to changes in surrounding temperature have potential application in a variety of fields, particularly those of controlled drug delivery and membrane application. Tanaka (Tanaka T., 1979) investigated the effect of temperature on polyacrylamide gels by fixing the acetone concentration in the swelling medium at about 40 % and changing the temperature. The behavior of the gels was similar to that seen by changing acetone concentration. At temperature above room temperature, the gels swelled. At room temperature the gels collapsed and remained collapsed while continuing to shrink below room temperature. These polyacrylamide gels were undergoing a coil-globule transition because of the reversible collapsing and expanding behavior they exhibited at specific acetone concentration and specific temperature.

Terpolymer gels of poly (N-isopropylacrylamide- ter-butylmethacrylate- ter-diethylaminoethyl methacrylate), poly(NIPAAm- ter-BMA-ter-DMAEMA) that exhibit temperature and pH sensitivity have also been studied by Feil (Feil, H. et al. 1991). These gels showed pH and temperature sensitivity in their swelling behavior because of the protonizable groups on the DMAEMA comonomer. At low pH, the gels were highly swollen because the DMAEMA was protonized , while at high the swelling greatly decreased because the DMAEMA was not protonized. This sensitive behavior was sensitive to temperature in that as temperature was increased the transition pH was lowered.

2.3 Preparation of Microporous or Macroporous Hydrogels

Hydrogels may be synthesized in a number of "classical" chemical ways. These include one-step procedures like polymerization and parallel cross-linking of multifunctional monomers, as well as multiple step procedures involving synthesis of polymer molecules having reactive groups and their subsequent cross-linking, possibly also by reacting the polymers with suitable cross-linking agents. (Brasch U. and Burchard W. 1996)

The bulk polymerization, i.e., polymerization in the absence of added solvent, of monomers to make a homogeneous hydrogel produces a glassy, transparent polymer matrix which is very hard. When immersed in water, the glassy matrix swells to become soft and flexible.

Although it permits the transfer of water and some low-molecular-weight solutes, such a swollen polymer matrix (hydrogel) is considered non-porous. The pores between polymer chains are in fact the only spaces available for the mass transfer, and the pore size is within the range of molecular dimensions (a few nanometers or less). In this case, the transfer of water or other solutes is achieved by a pure diffusion mechanism, which restricts the rate of absorption and to some extent the size of species that are absorbed. Homogeneous hydrogels have been used widely in various applications, especially in the controlled drug delivery area where limited diffusional characteristics are required.

Porous hydrogels are usually prepared by a solution polymerization technique, which entails polymerizing monomers in a suitable solvent. The nature of a synthesized hydrogel, whether a compact gel or a loose polymer network, depends on the type of monomer, the amount of diluent in the monomer mixture, and the amount of cross linking agent and/or delivered energy. As the amount of diluent (usually water) in the monomer mixture increases, the pore size also increases up to the micron range. Hydrogels with effective pore sizes in the 10-100 nm range and in the 100 nm-10 μm ranges are termed "microporous" and "macroporous" hydrogels, respectively. In practice, the terms "microporous" and "macroporous" are used interchangeably simply due to the fact that there is no unified definition of micro- and macro-pores in hydrogels. Accordingly, hydrogels having pores up to about 10 μm can be called either microporous or macroporous.

Porous hydrogels can be made by preparing hydrogels (usually from polymerizable monomers) in the presence of dispersed water-soluble porogens which can be removed later by washing with water to leave an interconnected meshwork (i.e., porous hydrogels). Examples of effective porogens are sucrose, lactose, and dextrin, sodium chloride, and poly (ethylene oxides) (PEGs). (Badiger M.V., et al., 1993)

Water itself can be used as a porogen if a polymer network is formed in the frozen state. Monomers can be polymerized in the frozen state around aqueous crystals, and then water can be subsequently removed by thawing to result in a macroporous hydrogel. In this approach, which is appropriately called a "freeze-thaw" technique (Kabiri, K., et. al., 2003), ice crystals function as the porogen. When a polymer network is formed in an aqueous solution, the whole system can be freeze dried to sublimate ice crystals and leave a porous matrix. This "freeze-drying" technique is useful in the preparation of porous hydrogels from water-soluble polymers such as polysaccharides (e.g., sodium alginate). To prepare porous hydrogels more effectively using the freeze-drying technique, salt can be added as another porogen, and this increases the reproducibility of preparing porous materials.

Non-aqueous solutions can also be used as porogens in polymerization of an oil-in-water emulsion system. In this case, the water phase contains water-soluble monomers and a cross-linker and the oil phase is a volatile organic solvent. The continuous water phase is polymerized and this is followed by evaporation of the oil phase, which results in the porous structure.

The pore size of hydrogels prepared by the porogen technique depends on the size and amount of the porogens. The introduction of a porogen reduces mechanical strength significantly, although a negative effect on the mechanical properties can be minimized if the size of the porogen is maintained below about 40 nm. In many cases where larger pores are necessary, microparticulate particles (e.g., sucrose crystals) can be used. The presence of such large sized pores will obviously make the porous hydrogels extremely weak.

In a solution polymerization, the monomers are usually mixed in a diluent which is good for both monomers and polymers. If, however, the diluent is a non-solvent for the polymer formed (e.g., PHEMA in water), the solubility of polymers dramatically decreases as the polymerization proceeds. This result in phase separation of the

polymer-rich monomer phase into droplets, which then join together to form a network filled with large spaces (i.e., heterogeneous, porous hydrogels) by the end of the polymerization process. This process is called heterogeneous solution polymerization (Dusek K. and Sedlacek B., 1969).

Phase separation can also be induced from the initially homogeneous polymer solution by altering the solvent quality. The solvent quality can be decreased by removing good solvent or adding non-solvent to a polymer solution or by changing the temperature. Many polymer solutions form a reversible gel upon changes in temperature. For example, gelation in water becomes a gel when cooled below the critical miscibility temperature. In general, aqueous polymer solutions can be rapidly frozen to result in spinodal decomposition and subsequent removal of water by freeze-dry sublimation yields porous hydrogels.

For polymers with a lower critical solution temperature (LCST), water becomes a non-solvent to the polymer and phase separation occurs as the temperature is increased above the LCST. This technique has been used to prepare porous hydrogels made of poly (N-Isopropylacryl amide), poly (methyl vinyl ether), (Şahiner, N., et. al., 2000) and others. The pore sizes of macroporous hydrogels prepared by phase separation are typically only a few micrometers. In addition, the overall porosity is very low and this implies that the pores are not well interconnected. The major limitation of the phase separation method is that only very limited types of porous hydrogels can be prepared. In addition, there is not much control over the porosity of the gels when prepared by phase separation.

Additionally, individual hydrogel particles can be surface cross-linked to form cross-linked aggregates of particles, thereby forming pores between the hydrogel particles. Such aggregate macrostructures are prepared by initially mixing the hydrogel particles (in the range of a few hundred micrometers) with a solution of a cross-linking agent, water, and hydrophilic organic solvent such as isopropanol (Rezai E. et al., 1994).

Pores in such structures are present between hydrogel particles and the size of the pores is much smaller than the size of the particles. This approach is limited to absorbent particles having chemically active functional groups on the surface.

It is important to distinguish the microporous and macroporous structures of hydrogels with those of non-hydrogel porous materials, such as porous polyurethane foams. In the plastic foam area, micro- and macro-pores are

indicated as having pores less than 50 μm and pores in the 100-300 μm range, respectively. One of the reasons for this difference is that hydrogels with pores larger than 10 μm were rarely made, while porous plastics having pores in the 100-300 μm range are very common. Porous hydrogels with a pore size larger than 100 μm were made by (Park H. and Park K. 1994), and that is probably why these definitions for porous hydrogels differ from those for porous plastics.

Microporous and macroporous hydrogels are sometimes called polymer "sponges". When a monomer, e.g., hydroxyethyl methacrylate (HEMA), is polymerized at an initial monomer concentration of 45 (w/w) % or higher in water, a hydrogel is produced with a porosity higher than the homogeneous hydrogels. These heterogeneous hydrogels are sometimes called "sponges" in the biomedical literature. The term "sponge" is not recommended, however, since it is better known as "rubber sponge" which is not a hydrogel in any sense. Moreover, the properties of rubber sponges are totally different from porous hydrogels. For example, rubber sponges release imbibed water upon squeezing, but porous hydrogels may not be squeezable - they may break into pieces with water entrapped in the polymer networks because of their hydrophilic nature.

Superporous hydrogel was developed approximately twenty years ago by Park for controlled delivery of drugs. Other researchers have recently extended the hydrogels for designing other drug delivery systems. So, creation of porosity in hydrogels is very important in many applications. In addition, several studies have been reported on aqueous solution polymerization at low monomer concentration. Data on concentrated aqueous solution polymerization are mostly reported as patents. Chen J. and Zhao Y., 1999, 2000) synthesized poly (sodium acrylate) water absorbent through concentrated (43.6 wt. %) aqueous solution by using potassium persulfate as an initiator. In last years, (Zohuriaan M., et al., 2003) focused on studying the synthesis and characterization of acrylic-based superabsorbents through solution and inverse-suspension methods. Following their previous works, they have recently emphasized mostly on the absorption rate enhancement through creating porosity. Formation of porous structure provides a certain way to improve the absorption rate. There are some methods for making porous structure in hydrogels such as phase separation technique, porogen technique and foaming technique. Oxley et. al have used foaming technique by applying acetone and sodium bicarbonate (SBC) as foaming agents. A water-

soluble crosslinker (N, N-methylene bisacrylamide, MBA) and an oil-soluble crosslinker (1,4-butanediol diacrylate, BDDA) have been used in the synthesis (Oxley, H.R., et. al., 1993).

One of the limiting factors of hydrogels has been the rather slow swelling property of dried hydrogels. For the dried hydrogels to swell, water has to be absorbed into the glassy matrix of the dried hydrogels. The swelling kinetics of the dried hydrogels thus depend on the absorption of water occurring by a diffusional process and the relaxation of the polymer chains in the rubbery region. Equilibrium swelling of dried hydrogels in an ordinary tablet size (e.g., 1 cm in diameter times 0.5 cm height) usually takes at least several hours, and this may be too slow for many applications where fast swelling is essential. For example, hydrogels have been successfully used as a gastric retention device that can stay in the stomach of a dog for up to 60 hours (Shalaby W.S.W. et al., 1992). In those studies, however, hydrogels had to be pre-swollen for a few hours before administering to the dog to avoid premature emptying into the intestine.

Although these methods allow obtaining products of desired properties, they have a significant drawback as far as synthesis of hydrogels for medical purposes is considered. Such products should not contain any toxic substances (monomers, initiators, cross-linking agents, and additives), that are normally used in the chemical procedures. These unwanted substances have usually to be washed out from the product in a separate step. This complicates the technology and may lead to a significant increase in production costs.

2.4 Radiation Synthesis of Hydrogels

Ionizing radiation has been long recognized as a very suitable tool for the formation of hydrogels (Güven O. and Şen M., 1991, Karadağ E., et al, 1996, Karadağ E., et al, 1995b, Saraydın D. et al 1995b, Saraydın D. et al 1995c, Rosiak J. M., 1991, 1994). Easy process control, possibility of joining hydrogel formation and sterilization in one technological step, no necessity to add any initiators, cross-linkers etc., possibly harmful and difficult to remove, no waste, relatively low running costs - this makes irradiation the method of choice in the synthesis of hydrogels, especially for biomedical use. Also from the point of view of radiation

chemistry, cross-linking of polymers, including hydrogel formation, belongs to the most successful applications of this branch of science.

Already in the early fifties, the pioneers of the radiation chemistry of polymers began some experiments with radiation cross-linking, also with hydrophilic polymers. However, hydrogels were analyzed mainly from the point of view of phenomena associated with mechanism of reactions, topology of network, and relations between radiation parameters of the processes. Fundamental monographs on radiation polymer physics and chemistry written by Charlesby (Charlesby A., 1960). and Chapiro (Chapiro A.; 1962) proceed from this time. The noticeable interest in application of radiation to obtain hydrogels for biomedical purposes began in the late sixties as a result of the papers and patents published by Japanese and American scientists. Among others, the team of the Takasaki Radiation Chemistry Research Establishment headed by Kaetsu as well as Hoffman and his colleagues from the Center of Bioengineering, University of Washington have created the base for spreading interest in the field of biomaterials formed by means of radiation technique. Immobilization of biologically active species in hydrogel matrices, their use as drug delivery systems and enzyme traps as well as modification of material surfaces to improve their biocompatibility and ability to bond antigens and antibodies have been the main subject of their investigations (Hoffman A. S., 1981).

Hydrogels can be obtained by radiation technique in different ways, including irradiation of solid polymer, monomer (in bulk or in solution) or aqueous solution of polymer. The first method, i.e. irradiation of hydrophilic polymer in a dry form, (Nedkov E. and S. Tsvetkova; 1994) has some drawbacks. It may require special sample preparation (like pressing or melting), and some difficulties may be encountered in obtaining homogeneous macroscopic hydrogels. Moreover, it requires usually much higher doses of ionizing radiation to obtain a gel compared to irradiation in solution, and, furthermore, it may be difficult to remove fully the oxygen, that can promote unwanted side reactions. One of the reasons for the high gelation doses in dry state is that radiation-chemical yield of radicals, that are the precursors of cross-links, is usually lower than in aqueous solution. Also the restricted motion of the radical-bearing chains limits the effectiveness of cross-linking. One has to note, however, that from the necessity to use higher doses for gelation in the solid state it does not follow that more energy is needed for the

formation of an average link between the chains. Radiation doses are calculated as energy per mass unit of the system. It was assumed that gelation occurs when, on average, one cross-link is formed per each polymer chain (Charlesby A., 1960), it is obvious that more cross-links are needed for the gelation of 1 kg of a solid polymer sample, than for gelation of 1 kg of its dilute solution.

More frequently the method of monomer irradiation is applied (Güven O. and Şen M., 1991, Şen, M., et al., Güven, et al, 1999). In this technique polymerization takes place in the first stage, followed by cross-linking of the formed chains. This way is possibly most convenient when the chosen monomer is easily available but its polymer is not. Since many of the monomers used are harmful or even toxic (usually contrary to the corresponding polymers), particular care has to be taken when using this method for the formation of hydrogels for biomedical use to ensure that either all the monomer has reacted or its unreacted residues have been fully extracted afterwards, in a separate operation. Since during irradiation of monomer many consecutive and parallel reactions occur, the system is rather complicated and difficult for qualitative description, although some attempts were done (Tobita H., 1993(a) 1993(b)). It is a frequent practice to add some bifunctional monomer to the mixture to increase the efficiency of cross-linking. It has to be stressed that in many cases this synthesis method works very well. There are rare cases, like with poly(vinyl alcohol) gels, where it cannot be used because of the unstability of the monomer.

Especially convenient method of radiation-based synthesis of hydrogels is the irradiation of polymers in aqueous solution, since such systems, containing neither monomer nor cross-linking agents (otherwise frequently used to enhance gel formation), are easier to control and study. Also, with the application of this method, lower number of usually unwanted processes occurs, as e.g. homografting of monomer on a polymer chain that may lead to branched structures, and, last but not least, hydrogels formed in this way are suitable for biomedical use (certainly, provided that a proper polymer is chosen) with no need of further purification (Şen, M., et al, 2000, Şen, M., et al, 2001, M. Şen and Avcı E. N., 2005).

Typical examples of simple, synthetic polymers used for hydrogel formation by this method are poly (vinyl alcohol) - PVAL, polyvinylpyrrolidone - PVP, poly(ethylene oxide) - PEO, polyacrylamide - PAAm, poly(acrylic acid) - PAA and poly(vinyl

methyl ether) - PVME. Gels obtained from two latter substrates belong to the group being of particular interest as the components of ”intelligent biomaterials”, since their properties are sensitive to environmental stimuli - pH, ionic strength (PAA) and temperature (PVME).

3. CHARACTERIZATION OF NETWORK STRUCTURE OF HYDROGELS

3.1 Swelling and Determination of Molecular Weight Between Cross-links

One of the basic parameters that describes the structure of a hydrogel network is the molecular weight between cross-links, $\overline{M}_c$ for highly swollen network (Güven O., and Şen M., 1998). This describes the average molecular weight of polymer chains between two consecutive junctions. These junctions may be chemical cross-links, physical entanglements, crystalline regions, or even polymer complexes. Several theories have been proposed to calculate the molecular weight between cross-links in a hydrogel. Probably the most widely used of these theories is that of (Flory, J. P., 1953). This earliest theory describes the equilibrium swelling characteristics of a cross-linked polymer system where the polymer chains are reacted in the solid state and the chains exhibit a gaussian distribution. This theory deals with neutral polymer chains and tetrafunctional cross-linking within the polymer gel. From swelling expression the average molecular weight between consecutive cross-links, $\overline{M}_c$ can be expressed by eqs. (3.1), (3.2), these equations have been widely used to characterize a variety of networks. Eqs. (3.1) and (3.2) were used when the networks were prepared from polymer and monomer or monomer mixtures, respectively (Labana S. S., 1987).

$$\frac{1}{\overline{M}_c} = \frac{2}{Mn} - \frac{\left(\bar{v}/V_1\right)\left[\ln(1-\upsilon_{2m}) + \upsilon_{2m} + \chi\upsilon_{2m}^2\right]}{\left[\upsilon_{2m}^{1/3} - \frac{\upsilon_{2m}}{2}\right]} \qquad (3.1)$$

$$\frac{1}{\overline{M}_c} = -\frac{\left(\bar{v}/V_1\right)\left[\ln(1-\upsilon_{2m}) + \upsilon_{2m} + \chi\upsilon_{2m}^2\right]}{\left[\upsilon_{2m}^{1/3} - \frac{\upsilon_{2m}}{2}\right]} \qquad (3.2)$$

Where $\overline{M}_n$ is the number average molecular weight of starting polymer, $\bar{v}$ is the specific volume of the polymer, V_1 is the molar volume of the swelling agent, υ_{2m} is the polymer volume fraction in the equilibrium-swollen system and χ is the Flory

polymer-solvent interaction parameter.

The Flory-Rehner model describes the situation in which cross-links are introduced in the dry stage. Peppas and Merrill (Peppas N.A., and Merrill E.W., 1976) derived a model which accounts for the introduction of cross-links in the swollen state as in the case of solution polymerization.

Flory-Rehner and Peppas-Merrill models describe the molecular weight between cross-links for neutral polymer networks but hydrogels may be neutral or ionic in nature. If the polymer chains making up the network contain ionizable groups, the forces influencing swelling may be greatly increased due to localization of charges within the hydrogel (Flory P.J., 1953). Ionic polymer networks in aqueous salt solutions yield a far more complicated situation than that of neutral polymers. The equilibrium swelling ratios attained are often an order of magnitude larger than those of neutral networks, as intermolecular interactions such as coulombic, hydrogen-bonding, and polar forces are present. Brannon-Peppas and Peppas have derived equations to describe this ionic contribution term for both anionic and cationic hydrogels. The theoretical swelling predictions based on these equations are well described by these researchers. Brannon-Peppas and Peppas(1991)

The molecular treatment of rubberlike elasticity has been improved by Flory and Erman approximately twenty years ago.(Mark J. E., and Erman B., 1988) including detailed swelling-structure relationship. These relationships, theories and the results are reviewed by Queslel and Mark J.E.(1983) and Mark J.E. and Erman B.(1988), for the characterization of model and randomly cross-linked networks. A combined evaluation of the approaches of Peppas et al. and Erman at al. are later considered and predictive equations for the swelling of hydrogels containing diprotic acid moieties are derived in the recent studies of Güven and Şen (Güven O., and Şen M., 1998).

In recent years rubberlike elasticity and uniaxial deformation experiments have been used for the characterization of various types of polymeric systems by many researchers. The basic principles of elasticity and deformation and it's use for the determination of molecular weight between cross-links ($\overline{M}_c$) and cross-link density of polymers are explained in details chapter four.

3.2. Determination of the Mesh Size

A structural parameter that is often needed when applying hydrogels in medicine and pharmacy and especially when determining their diffusive characteristics is the mesh size. The mesh size broadly defines the space between macromolecular chains in a cross-linked network and it is usually characterized by the correlation length, or distance, between two adjacent cross-links. An approximate method for its calculation is straight forward and has been discussed by Korsmeyer and Peppas (Korsmeyer, R. W. and Peppas, N.A., 1981**)** and Peppas (Peppas N. A., and Mikos A.G. 1986). In this thesis, the network mesh size, ξ, was calculated using eq. 3.3

$$\xi = \nu_{2m}^{-1/3}\left[C_n\left(\frac{2\overline{M}_c}{M_r}\right)\right]^{1/2}\lambda \qquad (3.3)$$

In this expression, C_n is the Flory Characteristic ratio or rigidity factor and λ is the carbon-carbon bond length(1.54 Å), M_r is the molecular weight of monomeric unit.

4. MECHANICAL PROPERTIES OF POLYMERS

4.1. Elasticity and Deformation

An important property of many structural materials is their ability to regain their original shape after a load is removed. These materials are called elastic. The degree of elasticity or "stiffness" of a material is called its Modulus of Elasticity (G). Given the modulus of elasticity, possible deformations can be calculated for any material and loading.

Robert Hooke, a great English scientist, during his investigations on the springs, discovered in elastic materials that, stress and strain are proportional. He first presented this in a lecture in 1678 and it is known today simply as Hooke's Law.

The English physician and physicist Thomas Young noted that if stress is proportional to strain, then for any given material, stress divided by strain would be a constant. This constant is known today as Young's Modulus or the Modulus of Elasticity and it is represented by:

$$G = \text{Stress}/\text{Strain}$$

The stress on a material is defined as the force per unit area as the material is stretched/compressed.

$$\text{Stress} = \text{Force}/A_o$$

The cross-sectional area may change if the material deforms as it is compressed or extended so the area used in the calculation is the original undeformed cross-sectional area A_o. The units of stress are the same as those of pressure. We will use pascals, Pa, as the units for the stress. In the polymer literature, stress sometimes is expressed in terms of psi (pounds per square inch) (1 MPa = 145 psi).

The strain is a measure of the change in length of the sample. The strain commonly is expressed in one of two ways.

elongation: $\varepsilon = (L/L_o)-1$ or compression: $\varepsilon = 1-(L/L_o)$

extension ratio: $\alpha = (L/L_o)$. The strain is a unitless number.

Where L_0 and L are the lengths of the undeformed and deformed hydrogel during compression. A stress-strain curve is a plot of stress on the y-axis vs. strain on the x-axis (Fig. 4.1.a). Young's modulus can be determined (for a given strain rate) for

a polymer by determining the slope of a stress-strain curve at low (<1%) strain (Fig. 4.1.b). A higher value of the modulus indicates a more brittle material (i.e. glass, ceramics). A very low value represents a ductile material (i.e. rubber). The toughness of a material is the area under a stress-strain curve. The area under the curve then is proportional to the integral of the force over the distance the polymer compressed or extended before failure. This integral is the work (energy) required to compress or extend the sample. The toughness is a measure of the energy a sample can absorb before it ruptures.

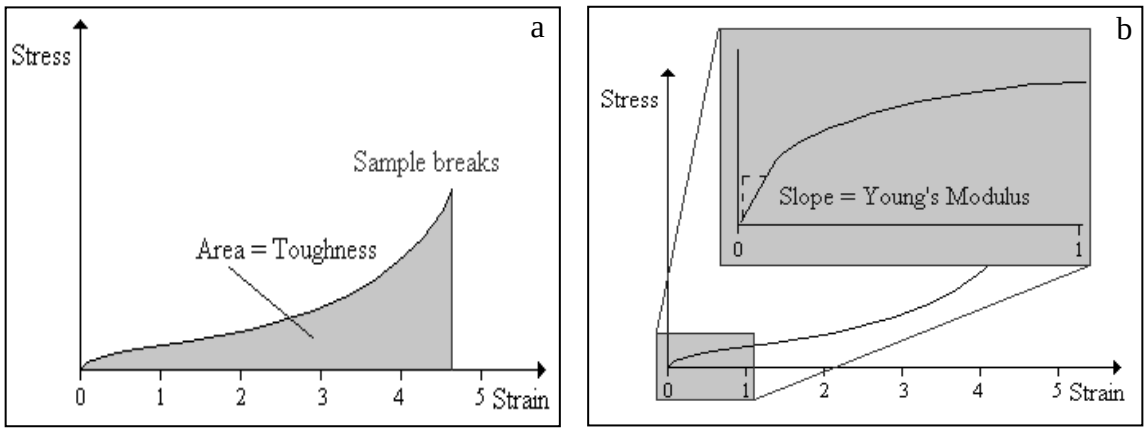


Fig.4.1. a) A typical stress-strain curve, b) Determination of Young's Modulus.

4.2. Stress Strain Behavior of Polymers

The Stress/strain behavior of solid polymers can be categorized into several classes of behavior: (Vishu, S., 1998).

1. Brittle fracture characterized by no yield point, a region of Hookean behavior at low strains and failure characterized by chonchoidal lines such as seen in inorganic glasses.

2. Yield behavior characterized by a maximum in the stress/strain curve followed by yielding deformation, which is usually associated with crazing, or shear banding and usually ductile failure. Ductile failure exhibits a high extent of deformation on the failure surface. Yield behavior can result in

necking, which exhibits a close to constant load regime and a terminal increase in the stress.

3. Rubber-Like behavior characterized by the absence of a yield point maximum but exhibiting a plateau in an engineering stress/strain curve. Often rubber-like behavior exhibits a terminal increase in the stress followed by failure, which results in a tear with little permanent deformation, exhibited in the failure surface.

There are a number of fundamental techniques used to characterize the mechanical properties of polymers, including tensile, flexural, compressive, tear strength, fatigue, impact, creep and hardness tests.

A soft but tough material shows low modulus and low yield stress, but very high elongation and high stress at break. Polyethylene is a classical example of these types of plastics. A hard and brittle material is characterized by high modulus and low elongation. It may or may not yield before breaking. One such type of polymer is general purpose phenolic. A hard and strong material has high modulus, high yield stress, high elongation at break, and high ultimate strength.

Table 4.1 and Fig. 4.2 summarize typical characteristics of Stress-Strain curves as it relates to polymer properties (Vishu, S., 1998).

Table 4.1. Characteristic features of stress-strain curves as it relates to polymer properties.

Description of Polymer	Modulus	Yield Stress	Ultimate Strength	Elongation at Break
Soft and weak	Low	Low	Low	Moderate
Soft and tough	Low	Low	Yield Stress	High
Hard and brittle	High	None	Moderate	Low
Hard and strong	High	High	High	Moderate

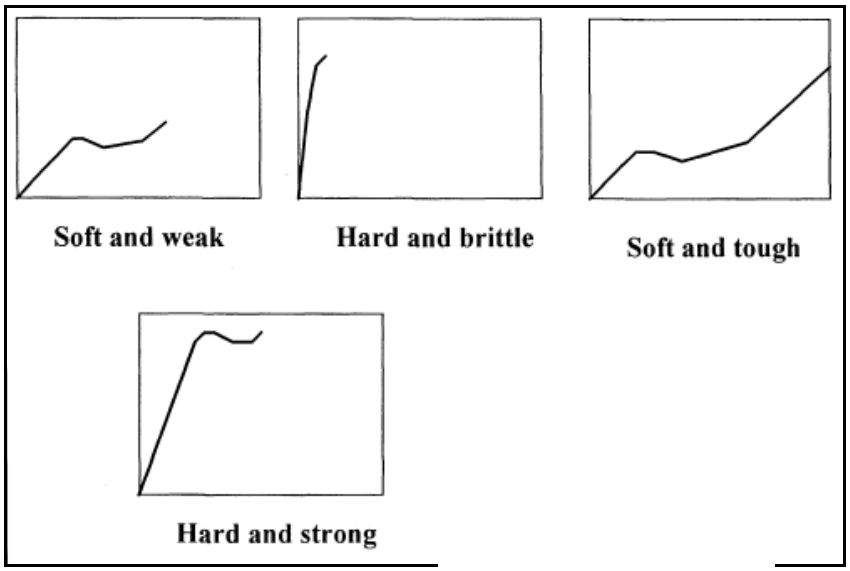


Fig. 4.2. Strain - stress behavior of solid polymers.

4.3. Uniaxial Compression of Polymers

Compressive properties describe the behavior of a material when it is subjected to a compressive load at a relatively low and uniform rate of loading. Compressive properties include modulus of elasticity; yield stress, deformation beyond yield point, compressive strength, compressive strain. Compression strength and modulus are tested, using ASTM D 695 procedures, by placing a specimen between two parallel platens and compressing it to rupture. Compressive strength is calculated by dividing maximum compressive load carried by the specimen during the test by the original minimum cross-sectional area of the specimen. The result is expressed modulus of elasticity or compressive modulus is also expressed by the slope of the initial straight-line portion of the stress-strain curve and is calculated by dividing the change in stress by the corresponding change in strain. Most engineering thermoplastics have high compression properties, which will only rarely place limitations on designs. In most cases, tensile or flexural strength impose many more constraints.

In recent years rubberlike elasticity and uniaxial deformation experiments have been used for the characterization of various types of polymeric systems by many researchers (Inci, M. N. et al., 2001, Okay, O. and Durmaz , S., 2002, Erman, B. and Mark, J. E., 1997, Uzun, C. et al., 2003).

Fig. 4.3 shows a typical stress–strain curve of hydrogels after compression test where the different mechanical parameters are specified. The coordinates of the point on the curve at which fracture of the gel sample occurred (i.e. maximum of the stress–strain curve) gives the stress and strain at fracture. Area below the curve until the fracture point gives the total energy (Toughness) required for fracture. The Young's compression modulus (ratio of stress to strain at small deformation) was calculated from the initial slope of the curve. The failure strain and failure stress were determined from compression curves as shown in Fig. 4.3. A large failure strain corresponds to a very deformable gel and a large failure stress indicates a strong gel.

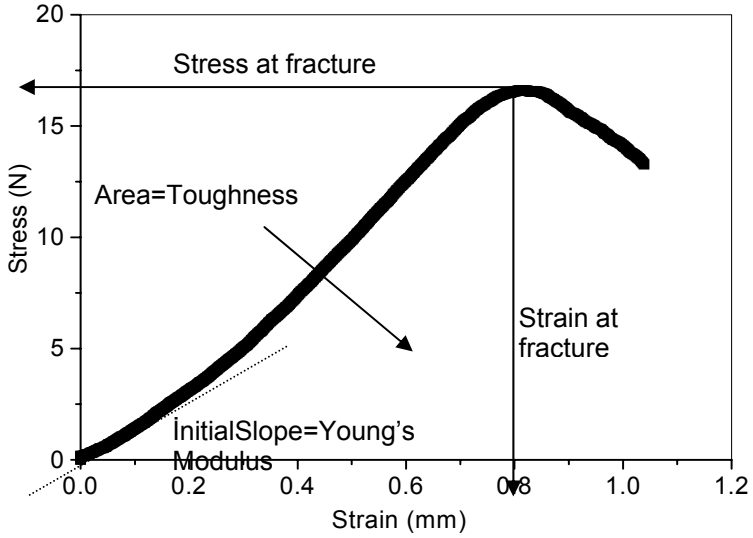


Fig. 4.3. Typical stress–strain curve of hydrogels in compression.

For uniaxial deformation, the statistical theories of rubber elasticity yield Eq. (4.1) for Gaussian chains.

$$f = G(\lambda - \lambda^{-2}) \qquad (4.1)$$

where f is the force acting per unit cross-sectional area of the undeformed gel specimen, G is the elastic modulus of the sample and λ is the deformation ratio (deformed length/ initial length). For a homogeneous network of Gaussian chains, the elastic modulus of gel swollen to equilibrium, G is related to the network cross-link density by Eq. (4.2)(Şen and Sarı, 2005).

$$G = A\frac{\rho}{\overline{M}_c} RT \upsilon_{2r}^{2/3} \upsilon_{2m}^{1/3} \quad (4.2)$$

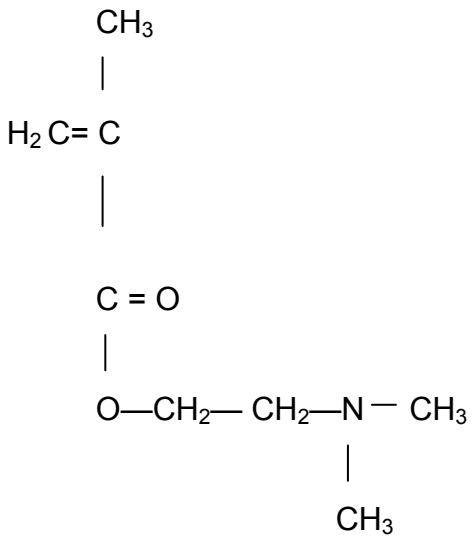
Where, ρ is the polymer density. The prefactor A, equals 1 for an affine network and $(1-2/\Phi)$ for a phantom network. υ_{2m} is the polymer volume fraction in the equilibrium-swollen system. υ_{2r} is the polymer volume fraction in the relaxed state i.e. after cross-linking before swelling and $\overline{M}_c$ is the molecular weight between cross-links. The effective cross-link density, ν_e of a cross-linked structure can be obtained from the results of compressive measurement:

$$\nu_e = \frac{\rho}{\overline{M}_c} \quad (4.3)$$

5. EXPERIMENTAL

5.1. Chemicals

The monomer used in this study, N, N dimethylaminoethyl methacrylate (DMAEMA) was obtained from Aldrich. The cross-linking agent ethylene glycol dimethacrylate (EGDMA) and pore forming agents NaCl and poly(rthylene glycol) with various molecular weight were obtained from Merck. K_2HPO_4 and KH_2PO_4 were used as buffer materials in the pH-swelling experiments were obtained from Fischer Scientific Company. The chemical formula of the DMAEMA is given in Scheme 5.1



Scheme 5.1.

5.2. Preparation of Hydrogels

Aqueous solutions of DMAEMA containing mixtures were prepared (5 ml DMAEMA / 1.5 ml water) and 0.05, 0.1, 0.5 and 1 .0 % EGDMA were added to the solutions. The density of DMAEMA is 0.933 g/cm^3. So the volume/volume ratios also can be assumed as weight to weight ratios. Monomer solutions thus prepared were placed in PVC straws of 4mm diameter and irradiated 4.0 kGy in Gammacell-220 type γ-irradiator at a fixed dose rate of 0.16 kGy/h. Hydrogels obtained in long cylindrical shapes were cut into pieces of 3-4 mm and stored.

For the preparation of DMAEMA hydrogels in the presence of NaCl 5 ml of

DMAEMA was mixed with 1.5ml 1.0, 2.0, 3.0 M NaCl solution and 0.5 % by volume EGDMA was added into these solutions. The solution was taken in PVC straws and irradiated 4.0 kGy.

For the preparation of DMAEMA in the presence of PEG 5 ml of DMAEMA was mixed with 1,5 ml 1.0 % , 5.0 % , 10.0 % , 20.0 % PEG solution and 0.05 % by volume EGDMA(volumeEGDMA/volumeDMAEMA) was added into these solutions. The molecular weight of PEGs used as diluents in the polymerization medium were 2000, 10000 and 20000 g/mol. The name of the initial mixtures and the amount of monomers and PEG used in these mixtures are given in Table 6.3 in details.

5.3.Determination of Percentage Gelation

Prepared gels were washed with distilled water to remove the uncross-linked polymer and/or residual monomer from the network structure and dried in air. The gels were then dried in vacuum oven until a constant weight was reached for each sample. Percentage gelation or percentage conversion of monomers and cross-linking agent into insoluble networks, was based on the total weight of the cross-linking agent and monomers present in the initial mixture.

5.4. Swelling Experiments

Dried hydrogels (2-3 mm thickness, 3mm diameter) were left to swell to investigate the swelling behaviour in various solutions and conditions. These solutions were various K_2HPO_4 and KH_2PO_4 phosphate buffer solutions at pH 3-8. Swollen gels removed from the swelling medium at regular intervals were dried superficially with filter paper, weighed and placed in to the same medium. The measurements were continued until a constant weight was reached for each sample. This weight was used to calculate the volume fraction of polymer, υ_{2m}, and the equilibrium degree of swelling (EDS), Q, of the gel swollen to equilibrium in aqueous solution.

5.5. Density Measurement

Density determination of samples was performed by means of Archimedes principle (buoyancy method). Archimedes principles stated that a body immersed in a liquid apparently loses weight by an amount equal to the weight of the fluid it

displaces. For this purpose a Mettler Toledo density kit was used on the Shimadzu Electronic balance (type AX200). The glass vessel of density kit was filled with n-hexane obtained from Merck.

The weight of samples were determined directly on electronic balance (w_1) and on the holder of density kit that immersed in n-hexane (w_2). The following equations are used for the determination of displaced n-hexane weight,

$$w_3 = w_1 - w_2$$

Where, w_3 is the weight of n-hexane displaced, w_1, is the weight of sample and w_2 is the weight of sample in n-hexane. The volume of the n-hexane displaced was calculated from the following equation.

$$V_{\text{n-hexane}} = w_3 / \rho_{\text{n-hexane}}$$

Where, $V_{\text{n-hexane}}$ is the volume of n-hexane and also the volume of the sample (V_s) and $\rho_{\text{n-hexane}}$ is the density of n-hexane.

The density of the sample (ρ_s) was calculated from the following equation by using w_1 and V_s values

$$\rho_s = w_1/V_s$$

5.6. FTIR Analysis

Fourier transform infrared (FT-IR) spectra were recorded by Nicolet 520 model FT-IR spectrophotometer in the range of 4000 and 400 cm^{-1}. Resolution for all infrared spectra was 4 cm^{-1} and 20 scan applied for each spectrum. In order to prepare the samples for FT-IR measurements, hydrogel was dried in vacuum oven, and then mixed with dry KBr. The percentage of polymer in KBr pellets was 10 (by weight).

5.7 Uniaxial Compression Test

The mechanical properties were determined at room temperature by uniaxial compression experiments at a crosshead speed of 5 mm/s until failure, using a Zwick Z010 model Universal Testing Instrument and uniaxial compression module, equipped with a 1 kN compression load cell. This apparatus consists of two stainless-steel flat discs, one of which is fixed while the other can be moved vertically. The diameter and height of each gel were measured with a compass prior to the test. The average value from a total of five measurements was used.

The mechanical properties of the hydrogels were measured in their relaxed state (after preparation).

The photographs of Universal Testing Machine and uniaxial compression module are given in Fig. 5.1.

The original data was recorded by Zwick test expert software. The % strain was calculated by this software from following equation

$$\%\,\text{Strain} = \frac{(L_0 - L)}{L_0} \times 100 \qquad (5.1.)$$

where L_0 and L are the lengths of the undeformed and deformed hydrogel during compression.

Fig. 5.1. The photographs of Universal Testing Machine and uniaxial compression module.

5.8. SEM Studies

The pore structures of hydrogels were monitored by using JeolJSM 5600 LVSEM model scanning electron microscope. For the SEM studies hydrogels were firstly swollen in pH 3 and pH 7 buffer solutions and then lyofilized at -50 $^{\circ}$C and 0.04 mbar. Surface of the all hydrogels coated with platinium/palladium mixture before scanning.

6.RESULT AND DISCUSSION

6.1. Preparation of PDMAEMA hydrogels

When pure N, N-dimethylamino ethyl methacrylate (DMAEMA) monomer was irradiated with gamma rays, polymerization and cross-linking reactions took place simultaneously. The total dose required for the onset gelation was determined to be 40 kGy for this system by Şen and Sarı (2005). The hydrogels prepared above this gelation dose showed low mechanical stability and ruptured upon swelling. This behavior was attributed to the presence of polymerized, but not cross-linked PDMAEMA chains entrapped in the gel structure. Their loss as sol fraction upon contact with water was naturally weakened the mechanical stability of the gel. For the DMAEMA irradiated at high doses i.e. 70 kGy, only 10% conversion from monomer to gel structure was observed.

In order to decrease the gelation dose and increase the cross-link density at the same time, 35 % water was added to the monomer and this solution was irradiated with γ-rays at different doses. It was observed that aqueous solution of DMAEMA monomer showed a very low tendency to cross-link when irradiated with gamma rays at low dose rates. The PDMAEMA hydrogels that were synthesized had poor mechanical stability, low % gelation (30 %) at even high doses such as 70 kGy. These results indicated that addition of 35 % water in the DMAEMA was not enough to improve the gelation of this monomer as observed for many vinyl type monomers (Saraydın D. et al, 1995(a), Güven O. and Şen M., 1991).

6.2. Preparation of P(DMAEMA/EGDMA) hydrogels

In order to further increase the percentage gelation and decrease gelation dose at the same time, a difunctional cross-linking agent, ethylene glycol dimethylacrylate (EGDMA) was added to the monomer/water mixture. As can be seen from Fig. 6.1. the percentage gelation of DMAEMA increases from 10 % to 97 % by the addition of only 0.1 % EGDMA in the aqueous solution of DMAEMA and increased slightly with the increasing of the cross-linking agent content. As mentioned above the aqueous solution of DMAEMA shows low % gelation at high doses such as 70 kGy. But in this study, addition of only a minute amount of EGDMA, the mixtures

reached very high % gelation (monomer to gel conversion) even at low doses such as 4 kGy.

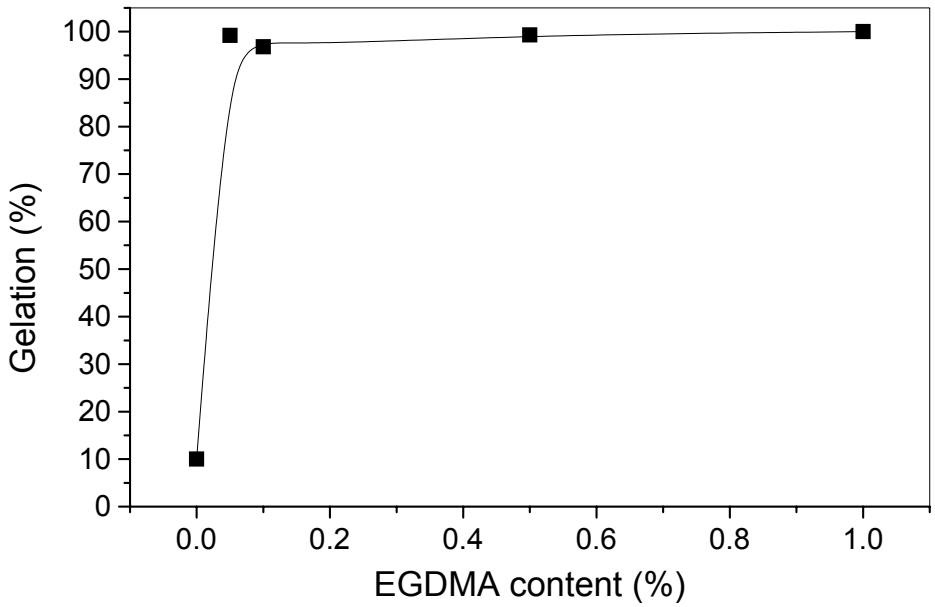


Fig. 6.1. The effect of cross-linking agent, EGDMA on the percentage gelation of DMAEMA. Total irradiation dose is 4 kGy.(The irradiation dose is 70 kGy for zero EGDMA concentration)

After preparation of hydrogels, firstly, FTIR spectra were taken. FTIR spectra of DMAEMA, EGDMA and P(DMAEMA/EGDMA) hydrogels containing 0.05 % EGDMA are given in Fig. 6.2. C=O band stretching peaks were observed at 1721 and 1723 cm^{-1} for DMAEMA and EGDMA respectively. The characteristic peak of ether group of EGDMA and carboxylate group of DMAEMA were observed at 1153 and 1165 cm^{-1} respectively.

For the investigation of the effect of cross-linking agent on the chemical structure of hydrogels, FTIR spectra of 0.05, 0.1, 0.5 and 1.0% EGDMA added pure DMAEMA hydrogels were scanned and this spectra are given in Fig. 6.3. As can be seen from the figures, the vinyl band at 1628-1640 cm^{-1} of monomers completely disappeared after irradiation. These results indicate that the polymerization reaction takes place by the opening of carbon-carbon double bond.

As can be seen Fig. 6.3, the FTIR spectra of various amount EGDMA containing hydogels are very similar. This was attributed to the very low concentration of EGDMA in the gel structure.

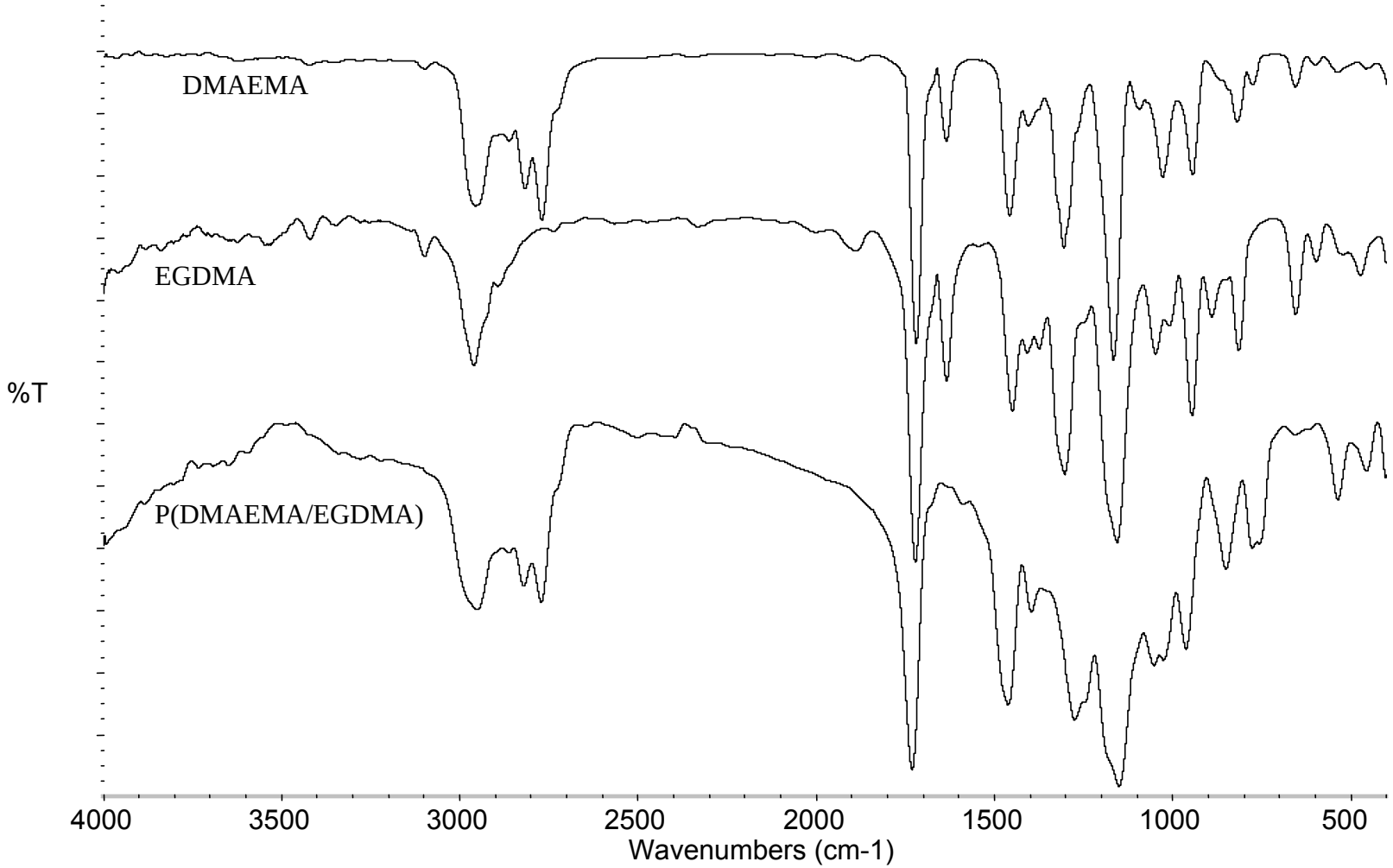


Fig. 6.2. FTIR spectra of pure DMAEMA, pure EGDMA and 0.05 % EGDMA containing P(DMAEMA/EGDMA) hydrogels.

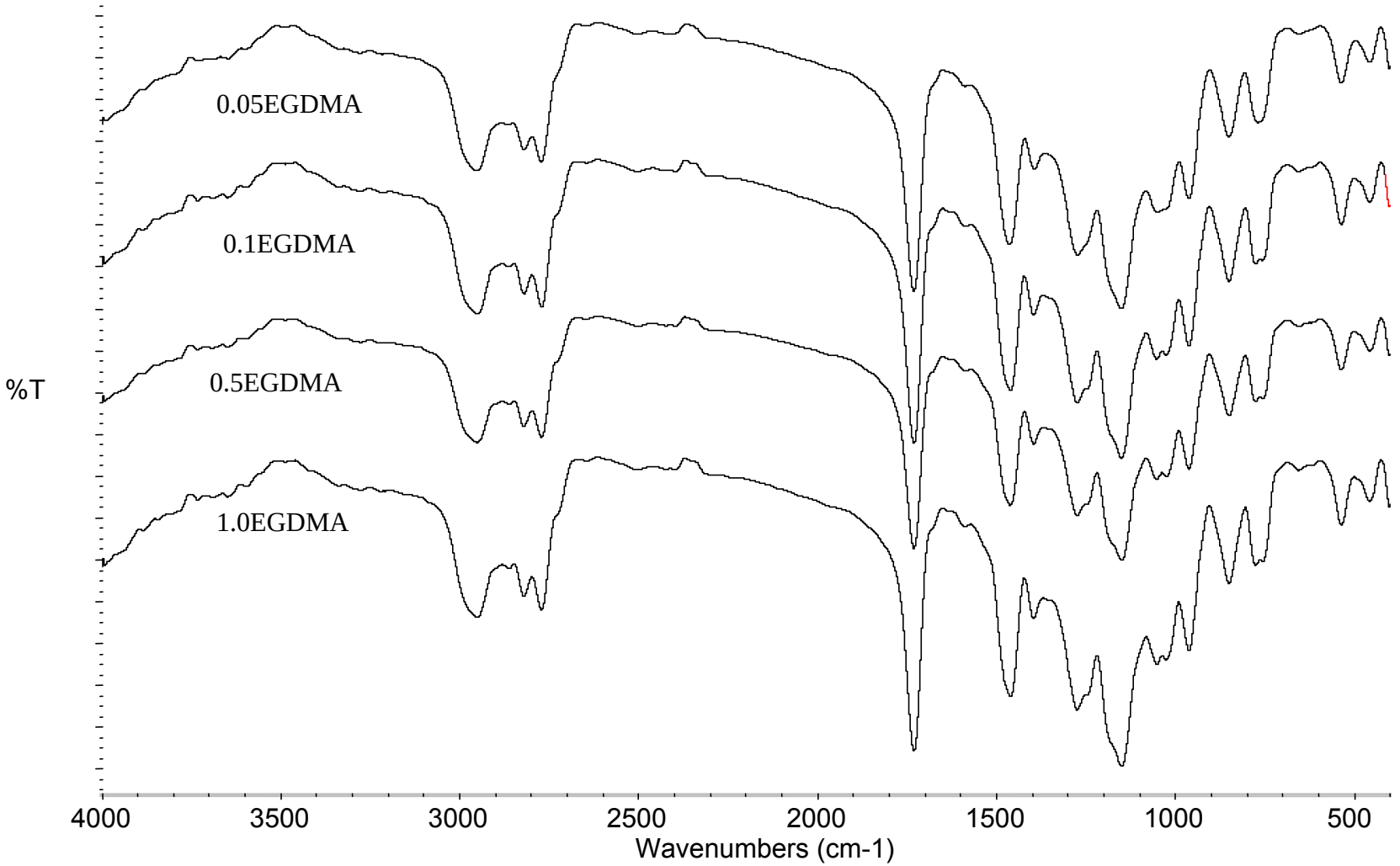


Fig. 6.3. FTIR spectra of 0.05, 0.1, 0.5, 1.0 % EGDMA containing P(DMAEMA/EGDMA) hydrogels.

6.3 Characterization of Network Structure of P(DMAEMA/EGDMA) Hydrogels

For the characterization of network structure and determination of molecular weight between cross-links, $\overline{M}_c$, of prepared hydrogels, the swelling properties at non-protonized state (pH7) were firstly investigated. Swelling experiments were continued until a constant value of swelling was reached for each sample. This weight was used to calculate the volume fraction of polymer ν_{2m} and the equilibrium volume swelling ratio, (V_s /V_d) (volume of swollen gel / volume of dry gel) by using Eq. 6.1

$$\frac{1}{\upsilon_{2m}} = \frac{V_s}{V_d} = 1 - \left[1 + \frac{\rho_{gel}}{\rho_w} \left(w^{-1} - 1 \right) \right] \qquad (6.1)$$

Here, V_d is the volume of dry polymer sample and V_s is the gel sample volume after equilibrium swelling, ρ_{gel} and ρ_w are the densities of dry gel and water respectively. Density of water is taken as 1 g/cm^3.

After swelling experiments, the uniaxial compression was applied using the Universal Testing Instrument on the swollen gels at pH 7. Typical stress-strain curves of P (DMAEMA/EGDMA) hydrogels are given in Fig. 6.4. In the notation used for the identification of samples, the numbers preceeding the abbreviations denote the percentage composition of EGDMA by volume. As can be seen from the figure, the magnitude of stress increased for a certain strain with increasing EGDMA content. During the determination of Elastic Modulus of a hydrogel system initial stages of deformation is important so experiments were stopped before complete deformation of the hydrogel system. Elastic modulus values of hydrogels were calculated by using elastic deformation theory and Eq. 6.2 (Mark J. E., and Erman B., 1988).

$$f = G(\lambda - \lambda^{-2}) \qquad (6.2.)$$

When the equation is applied to the initial stages of deformation, plots of f vs. (λ-λ^{-2}) yield straight lines, Fig. 6.5. Where, λ is deformation ratio and equal to L/L_0. L_0 and L are the length of the undeformed and deformed hydrogels during compression, respectively. The G value was calculated from the slope of lines and listed in Table 6.1.

In the slightly swollen state, the contraction junction theory indicate that a real network exhibits properties closer to the affine network model. Consequently Eq. 6.4 may thus be used to estimate the average molecular weight between cross-links.

Where, υ_{2r} is the polymer volume fraction in the relaxed state i.e. after cross-linked before swelling and $\overline{M}_c$ is the molecular weight between cross-links. For the determination of υ_{2r} weight fraction of polymer in freshly synthesized sample was used for w in Eq. 6.3. Here υ_{2r} is the volume of freshly synthesized sample and V_d is the gel volume of dry polymer.

$$\frac{1}{\nu_{2r}} = \frac{V_r}{V_d} = 1 - \left[1 + \frac{\rho_{gel}}{\rho_w}\left(w^{-1} - 1\right)\right] \tag{6.3}$$

By using *G* values and other relevant experimental parameters, $\overline{M}_c$ values were calculated by using Eq. 6.4. and collected Table 6.1.

$$G = \frac{\rho}{\overline{M}_c} RT \nu_{2r}^{2/3} \nu_{2m}^{1/3} \tag{6.4}$$

Table 6.1. Structural properties of P(DMAEMA/EGDMA) hydrogels

EGDMA (%)	ρ (g/cm^3)	ν_{2m}	ν_{2r}	*G* (kPa)	$\overline{M}_c$ (g/mol)	ξ (nm)
0.05	1.055	0.095	0.764	17	63480	22.6
0.1	1.058	0.149	0.750	33	37120	15.3
0.5	1.043	0.192	0.756	60	21820	10.9
1.0	1.052	0.247	0.777	166	8720	6.4

As can be seen from Table 6.1, the molecular weight between cross-links of P (DMAEMA/EGDMA) hydrogels decrease continuously with increasing amount EGDMA, from 0.05% to 1.0%.

One of the important parameters characterizing hydrogel systems is the mesh size. The mesh size characterizes the space in macromolecular cavity. In this thesis, the network mesh size, ξ, was calculated by using Eq. (6.5.)

$$\xi = \nu_{2m}^{-1/3}\left[C_n\left(\frac{2\overline{M}_c}{M_r}\right)\right]^{1/2}\lambda \qquad (6.5)$$

In this expression, C_n is the Flory Characteristic ratio and λ is the carbon-carbon bond length (1.54 Å), M_r is the molecular weight of the monomeric unit. The Flory characteristic ratio for the P (DMAEMA/EGDMA) hydrogels was not defined in the literature and determination of this parameter need long experimental procedures and using of different techniques. We made an assumption and used the C_n value of poly (acrylic acid) (6.7) for our systems.

Fig. 6.6 shows that the mesh size in P (DMAEMA/EGDMA) hydrogels decreased from 22.6 to 6.4 nm with the increase of cross-linking agent content from 0.05 to 1.0 % in the hydrogel structure

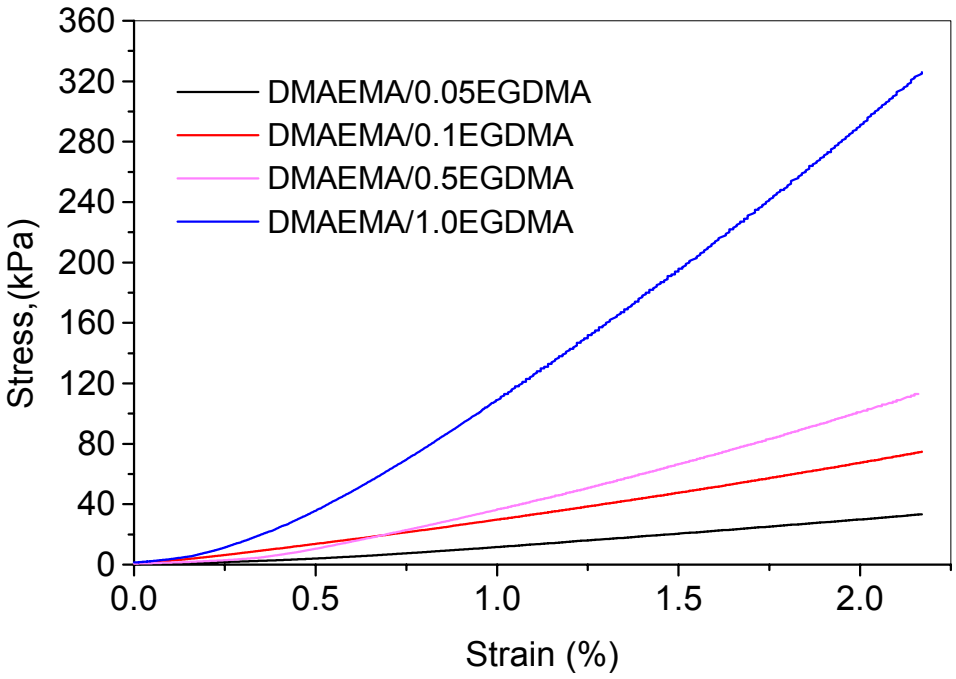


Fig. 6.4. Stress versus strain curves of 0.05 %, 0.1 %, 0.5 % and 1.0 % EGDMA containing P(DMAEMA/EGDMA) hydrogels.

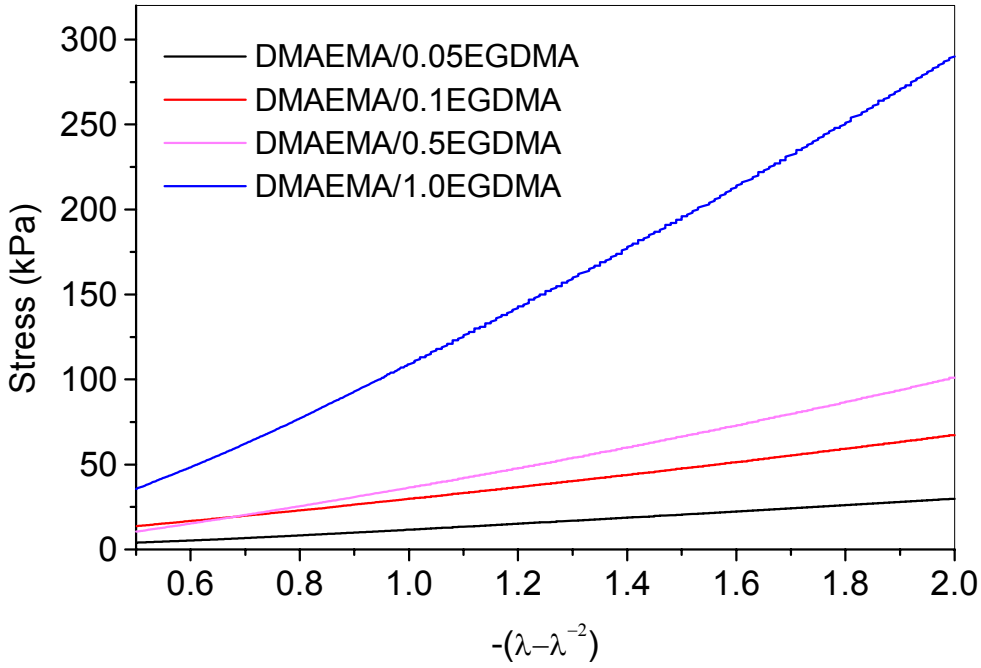


Fig. 6.5. Stress versus -(λ-λ^{-2}) curves of 0.05 %, 0.1 %, 0.5 % and 1.0 % EGDMA containing P (DMAEMA/EGDMA) hydrogels.

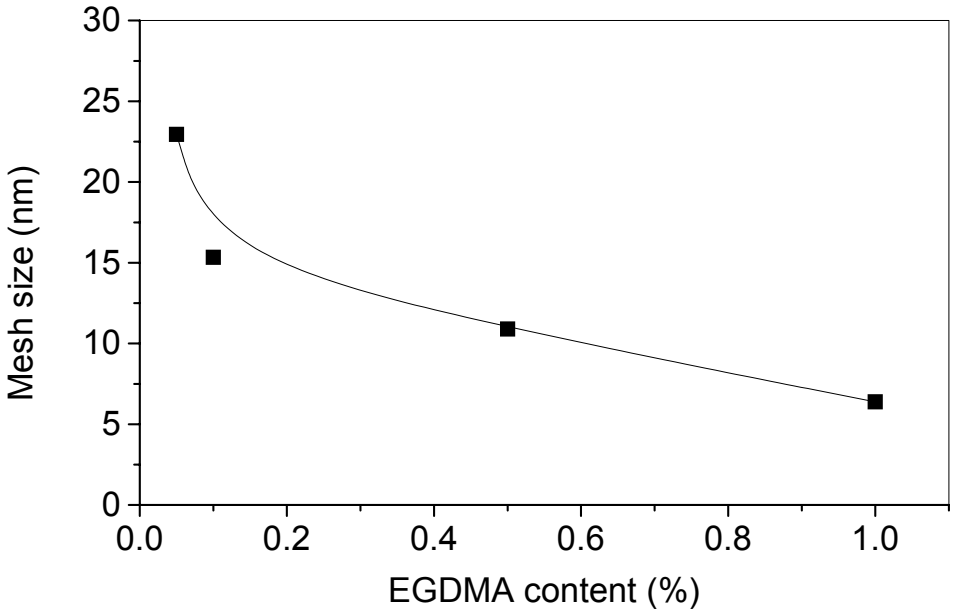


Fig. 6.6. Effect of cross-linking agent, EGDMA on the mesh size of P(DMAEMA/EGDMA) hydrogels.

6.4. Preparation of P(DMAEMA) Hydrogels in the Presence of NaCl

As explained in the introduction different techniques can be used to improve the pore size of hydrogel systems. In this study firstly we used NaCl. Aqueous sodium chloride solutions were used as diluents in the polymerization medium. For the preparation of NaCl containing initial mixtures 5 ml of DMAEMA was mixed with 1.5 ml 1.0, 2.0, 3.0 M NaCl solution and 0.5 % by volume EGDMA was added into these solutions. The solution was taken in PVC straws and irradiated 4.0 kGy. Hydrogels that were obtained in long cylindrical shapes, were cut into pieces of 3-4 mm and dried in a vacuum oven at 318 K to constant weight and subjected to Soxhlet extraction for three days with cold and hot water. Uncross-linked polymer and/or residual monomer and NaCl were removed during this extraction from the gel structure. Fig. 6.7 shows the effect of NaCl on the gelation of DMAEMA. As can be seen from the figure, NaCl does not affect the % gelation of DMAEMA. In order to explain the effect of NaCl on the network structure, the molecular weight between cross-links and mesh size were calculated. After swelling experiments done at pH 7 the uniaxial compression was applied using the Universal Testing Instrument. Stress-strain curves of P(DMAEMA) hydrogels prepared in the presence of NaCl were given in Fig. 6.8. Fig.6.9 was obtained by evaluation of Fig 6.8 and *G* values of hydrogels were calculated from the slope of the lines given in Fig 6.9. *G* values and other relevant experimental parameters were used to calculate the $\overline{M}_c$ values by using Eq. 6.4 and collected in Table 6.2.

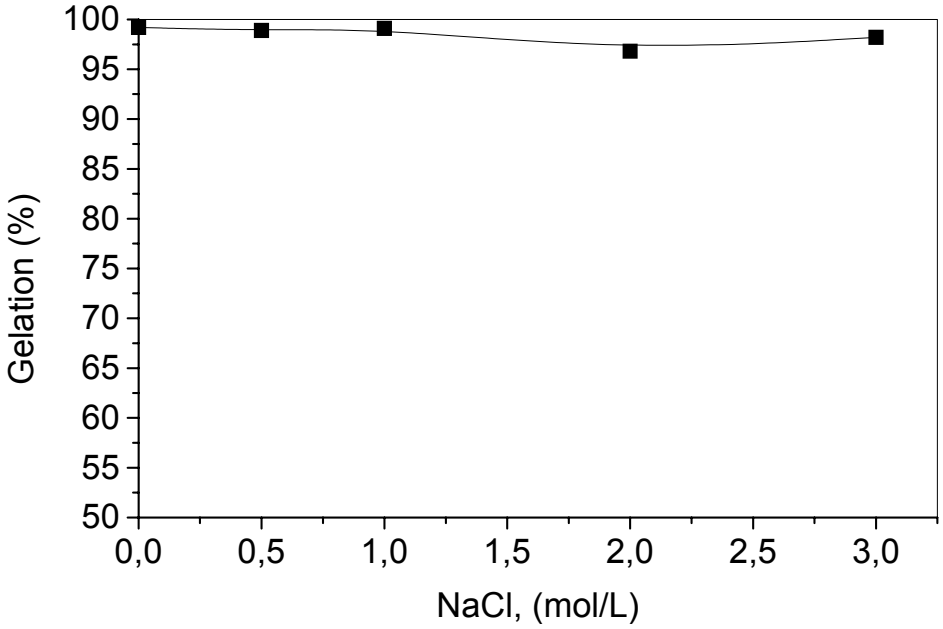


Fig. 6.7. The effect of NaCl on the percentage gelation of DMAEMA. EGDMA content in the initial mixture is 0.5%.

Table 6.2. Structural properties of PDMAEMA hydrogels prepared in the presence of NaCl

Gel name	ρ (g/cm^3)	ν_{2m}	ν_{2r}	G (kPa)	$\overline{M}_c$ (g/mol)	ξ (nm)
P(DMAEMA)/0NaCl	1.055	0.095	0.764	17	63480	10.9
P(DMAEMA)/1NaCl	1.058	0.094	0.756	67	1420	3.4
P(DMAEMA)/2NaCl	1.054	0.114	0.756	75	1630	3.5
P(DMAEMA)/3NaCl	1.052	0.127	0.756	86	1640	3.4

As can be seen from Table 6.2., the molecular weight between cross-links of PDMAEMA hydrogels sharply decreased by adding 1 M NaCl solution into initial mixture. NaCl was added in the initial mixtures as diluent and we expect that pore size of hydrogel will be improved by the addition of it (L., Quing et. al.,2000). However, it has been observed that NaCl decrease the mesh size of hydrogel.

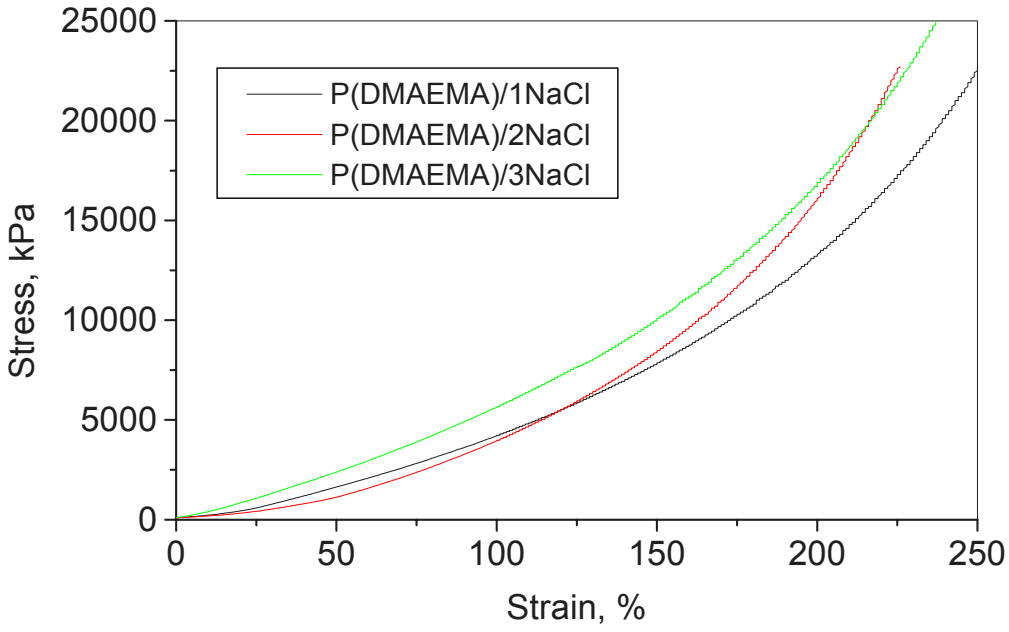


Fig. 6.8. Stress versus strain curves of PDMAEMA hydrogels prepared in the presence of NaCl.

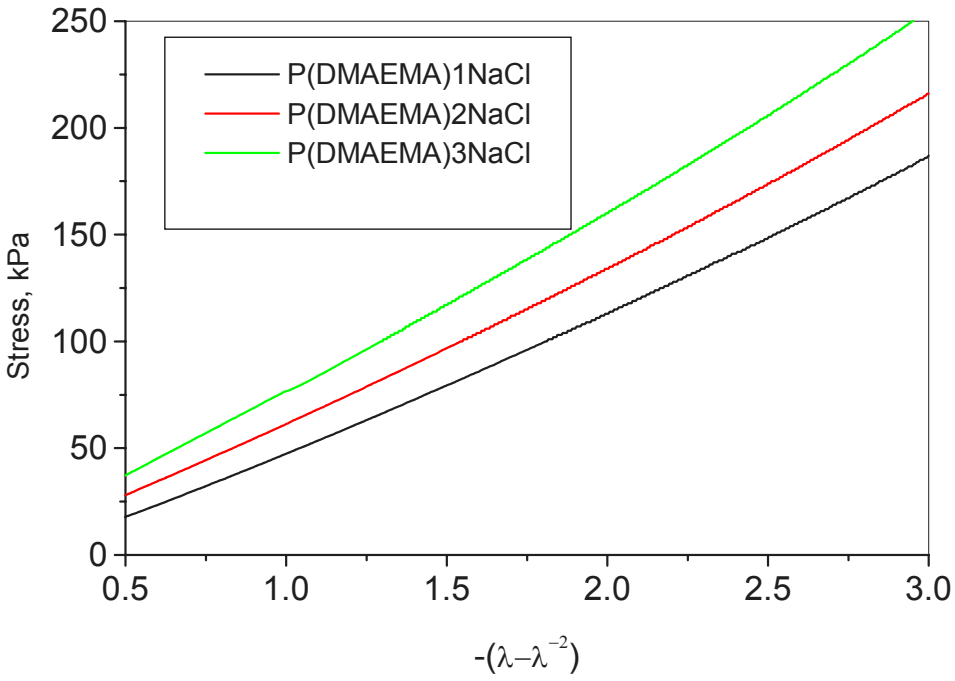


Fig. 6.9. Stress versus $-(\lambda-\lambda^{-2})$ curves of PDMAEMA hydrogels prepared in the presence of NaCl

The variation of the mesh size of PDMAEMA hydrogel with NaCl concentration is given in Table 6.2. As can be seen from the Table, the mesh sizes of the hydrogels decrease from 10.4 to 3.4 nm when NaCl concentration is increased from 0 to 1 M irrespective of NaCl concentration in the initial mixture.

Approximately three fold decrease in the pore size of PDMAEMA hydrogels with the addition of 1M NaCl in the initial mixture instead of water was attributed to the shrinking of chains, providing increased intermolecular contacts. Similar effects during the adsorption of Ca^{2+} and Na^{+} ions to poly (arylic acid) based hydrogels were observed by Khare and Peppas and known since long. (Khare A. R. and Peppas N. A. 1994).

The main aim of this thesis is the synthesis of mechanically stable %100 gelled PDMAEMA hydrogels having large pores. For this purpose we added NaCl into the initial mixture but we observed that NaCl couldn't create macro pores on the contrary the cross-link density was increased.

In order to increase the pore size of PDMAEMA hydrogels, secondly, we prepared initial mixtures from the ternary mixtures of DMAEMA/EGDMA and aqueous solution of low molecular weight PEGs. The experimental studies performed with these mixtures are given in the next part.

6.5. Preparation of P(DMAEMA) Hydrogels in the Presence of Poly(ethylene glycol) (PEG)

As mentioned above NaCl wasn't sufficient to improve the pore size of PDMAEMA hydrogels. In order to increase the pore size of hydrogels we added water soluble low molecular weight poly(ethylene glycols) into the initial mixtures. For the preparation of PEG containing mixtures, 5 ml of DMAEMA was mixed with 1,5 ml 1.0 % , 5.0 % , 10.0 % , 20.0 % PEG solution and 0.05 % by volume EGDMA (volume EGDMA /volume DMAEMA) was added into these solutions. The molecular weight of PEG' s used as a pore forming agent in the polymerization medium were 2000, 10000 and 20000 g/mol. The code of the initial mixtures and the amount of monomers and PEG used in these mixtures are given in Table 6.3.

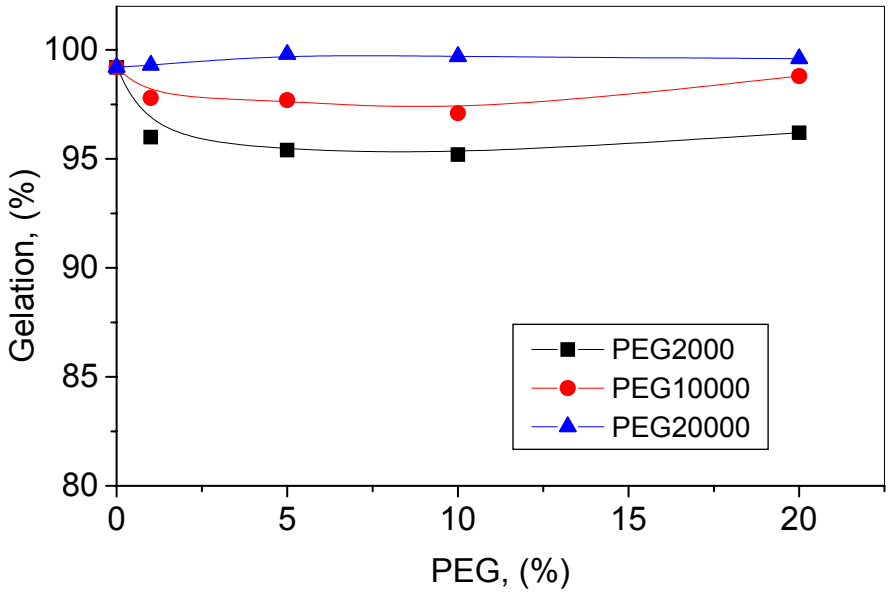
Table 6.3 The code abbreviation of prepared hydrogels and the amount of the components used in the preparation of these gels.

Gel Code ***(DMAEMAXPEGY)***	*Composition of hydrogel* DMAEMA *(ml)*	EGDMA *(µl)*	PEG solution *ml : %*	Mol. Weight of PEG *(kD)*
DMAEMA1PEG2	5.0	0.05	1.5 : 1.0	2
DMAEMA5PEG2	5.0	0.05	1.5 : 5.0	2
DMAEMA10PEG2	5.0	0.05	1.5 : 10.0	2
DMAEMA20PEG2	5.0	0.05	1.5 : 20.0	2
DMAEMA1PEG10	5.0	0.05	1.5 : 1.0	10
DMAEMA5PEG10	5.0	0.05	1.5 : 5.0	10
DMAEMA10PEG10	5.0	0.05	1.5 : 10.0	10
DMAEMA20PEG10	5.0	0.05	1.5 : 20.0	10
DMAEMA1PEG20	5.0	0.05	1.5 : 1.0	20
DMAEMA5PEG20	5.0	0.05	1.5 : 5.0	20
DMAEMA10PEG20	5.0	0.05	1.5 : 10.0	20
DMAEMA20PEG20	5.0	0.05	1.5 : 20.0	20

* For the gel name X and Y represent the % of PEG solution from which 1.5ml was added into the initial mixture and the molecular weight of PEG as kD, respectively.

These solutions were taken in PVC straws again and irradiated 4.0 kGy. Hydrogels obtained in long cylindrical shapes were cut into pieces of 3-4 mm and subjected to Soxhlet extraction for three days with cold and hot water. Uncross-linked polymer and/or resudial monomer and PEG were removed during this extraction from the gel structure. Fig. 6.10 shows the effect of PEG concentration and molecular weight on the gelation of DMAEMA. Percentage gelation i.e. percentage conversion of monomer (DMAEMA), cross-linking agent (EGDMA) into insoluble networks, was based on the total weight of these two monomer in the initial mixture. As can be seen from the figure, PEG affects the % gelation of DMAEMA and gelation was decreased with the decrease of molecular weight of the PEG and with the increasing PEG content in the initial mixture.

After preparation of hydrogels, the FTIR spectra were taken by Nicolet model spectrometer. The FTIR spectrum of PEG2000 and non-washed and washed DMAEMA20PEG20 hydrogel are given Fig. 6.11. Two characteristic peaks of PEG at 1140 and 845 cm^{-1} were also observed for non-washed DMAEMA20PEG20 hydrogel as a sharp and shoulder peak respectively. However, these two peaks were disappeared in the spectrum of washed DMAEMA20PEG2 hydrogel. This indicates that PEG can be easily removed from the hydrogel system by washing. The FTIR spectra of washed DMAEMA/PEG hydrogels containing different percentages of PEG in the initial mixture having molecular weights of 2000, 10000, 20000 are given in Fig. 6.12-6.14. As can be seen from Fig. 6.13 the FTIR spectra of hydrogels are very similar to the spectrum of washed DMAEMA hydrogel given in Fig. 6.12. These results indicate that PEG10000 can also be removed from the gel structure like PEG2000 by washing. On the other hand, observation of these two characteristic peaks of PEG in the FTIR spectra of washed DMAEMA5PEG20, DMAEMA10PEG20 and DMAEMA20PEG20 hydrogels indicate that PEG20000 probably forms interpenetrating network with DMAEMA monomer. The higher percentage gelation of PEG 20000 used initial mixtures than PEG2000 and PEG 10000 used mixtures was attributed to this interpenetrated and/or grafted PEG molecules in the hydrogel systems.



SFig. 6.10. The effect of molecular weight of PEG and it's content in the initial mixture on the percentage gelation of DMAEMA. The EGDMA content in all initial mixtures is 0.05 %.

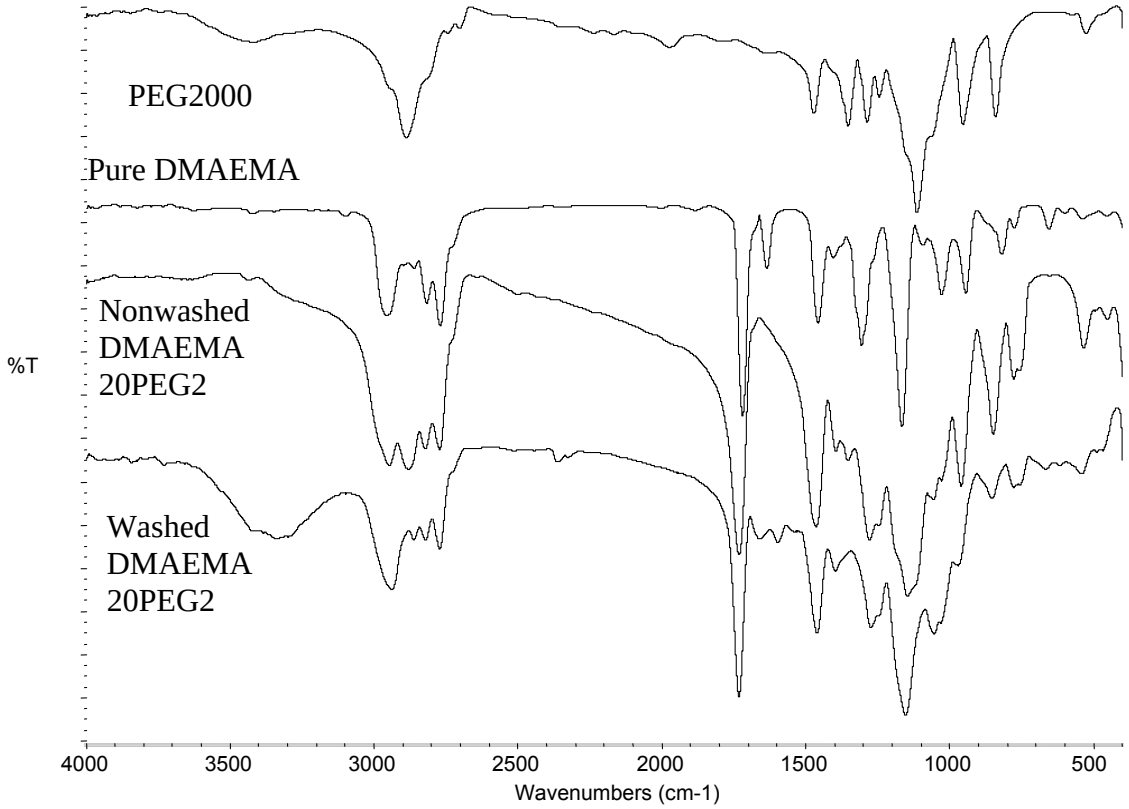


Fig. 6.11. FTIR spectra of PEG, DMAEMA, non-washed and washed DMAEMA20PEG2 hydrogel system.

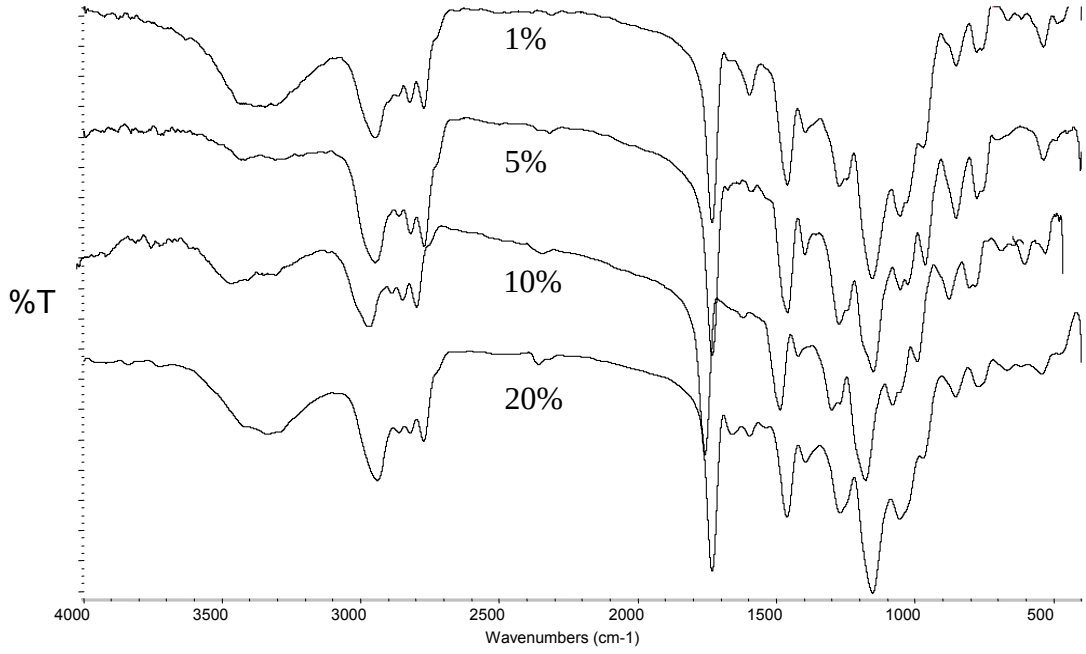


Fig. 6.12. The FTIR spectra of PDMAEMA hydrogels obtained by using 1%, 5%, 10% and 20% PEG2000 in the initial mixtures.

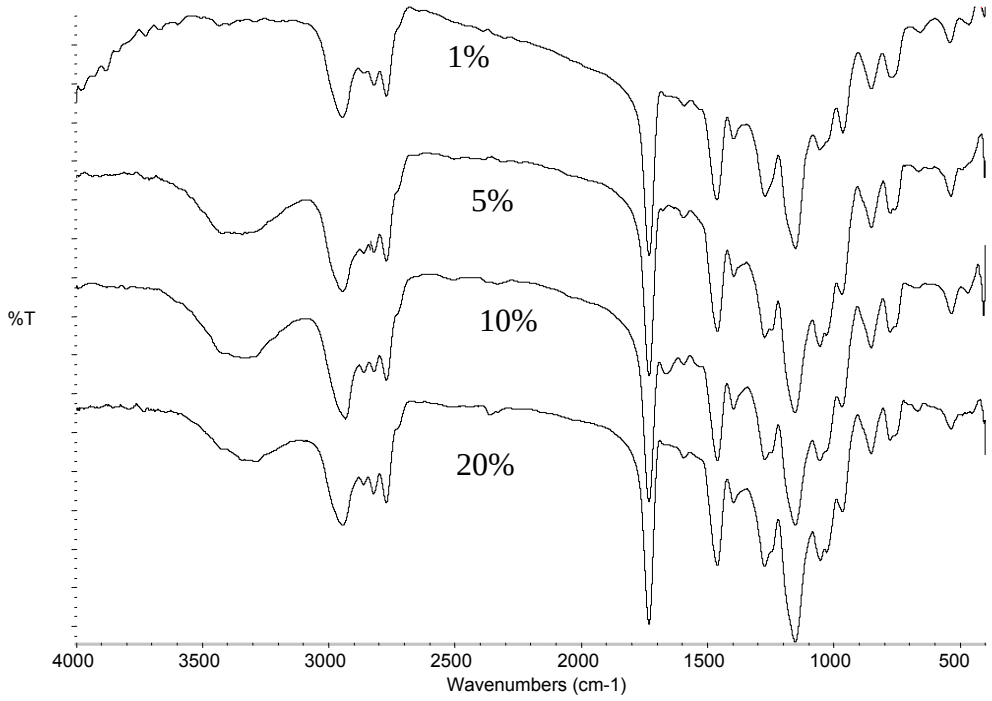


Fig 6.13. The FTIR spectra of PDMAEMA hydrogels obtained by using 1%, 5%, 10% and 20% PEG10000 in the initial mixtures.

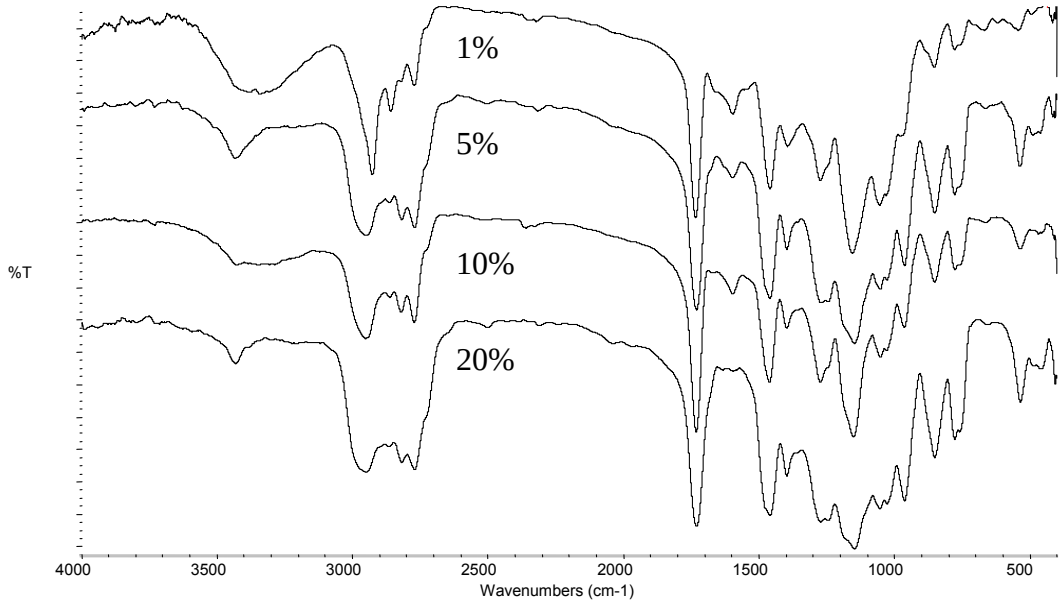


Fig. 6.14. The FTIR spectra of PDMAEMA hydrogels obtained by using 1%, 5%, 10% and 20% PEG20000 in the initial mixtures.

6.6. Characterization of Network Structure of DMAEMA Hydrogels Prepared in the Presence of PEG

For the characterization of the network structure and determination of the molecular weight between cross-links, $\overline{M}_c$, of DMAEMA hydrogels, the swelling properties at non-protonized state (pH7) were firstly investigated. Swelling experiments were continued until a constant value of swelling was reached for each sample. This weight was used to calculate the volume fraction of polymer υ_{2m} and the equilibrium volume swelling ratio, (V_s/V_d) (volume of swollen gel / volume of dry gel) by using Eq. 6.1.

After swelling experiments the uniaxial compression was applied using the Universal Testing Instrument on the gels swollen at pH 7. The stress-strain curves of DMAEMA hydrogels containing different percentages of PEG in the initial mixture having molecular weights of 2000, 10000, 20000 are given in Fig. 6.15-6.17.

In the notation used for the identification of samples, the numbers proceeding the abbreviation denote the percentage composition and the molecular weight of PEG (See Table 6.3). As can be seen from figure, the magnitude of stress decreased for a certain strain with increasing PEG content. During the determination of Elastic modulus of a hydrogel system initial stages of deformation is important so the experiments were stopped before the complete deformation of the hydrogel system. Elastic modulus values of hydrogels were calculated by using elastic deformation theory and Eq. 6.2

When the equation is applied to the initial stages of deformation, plots of f vs. $(\lambda-\lambda^{-2})$ yield straight lines, Fig. 6.18-6.20. The G value was calculated from the slope of lines and listed in Table 6.4. By using G values and other relevant experimental parameters, $\overline{M}_c$ values were calculated by using Eq. 6.3 and collected in Table 6.4.

Then, mesh size of PDMAEMA hydrogels were calculated by using Eq. 6.4 and plotted in Fig.6. 21. As can be seen from Table 6.4 and Fig. 6.21, during the preparation of DMAEMA hydrogels, addition of PEG decreased the cross-link density and increased the mesh size. The highest mesh size was reached with 20% of PEG having a molecular weight of 10000. Probably, due to formation of interpenetrating network structure or grafting the pore size of the hydrogels were

reduced for PEG20000 used system. Increasing the amount of PEG20000 in the initial mixture, mesh size was increased but this increase wasn't as sharp as for PEG2000 and PEG10000 except DMAEMA20PEG20 hydrogel system.

The aim of this study is to change the mesh size of DMAEMA hydrogels with the addition of some additives in the initial mixture. For this aim, different type hydrogels have been prepared until now by changing concentration of cross-linking agent (EGDMA) and NaCl, or percentage and molecular weight of PEG in the initial mixture. The effects of all these additives on the mesh size can be seen from figure 6.22. According to Fig. 6.22, mesh size of PDMAEMA hydrogel is 22.9 nm when EGDMA used is only 0.05 %. The mesh size decreased to 6.4 nm with increasing the content of cross-linking agent (EGDMA) from 0.05% to 1.0%. As mentioned above, addition of NaCl in the initial mixture decreased the mesh size and not changed significantly with increasing its concentration. But addition of PEG2000 and PEG10000 in the initial mixture the mesh size has been increased approximately two fold.

Table6.4. Structural properties of PDMAEMA hydrogels prepared in the presence of PEG.

	swelling (%)	(ρ) g/cm^3	(υ_{2m})	(υ_{2r})	G (kPa)	Mc (g/mol)	mesh size(nm)(ξ)
P(DMAEMA)/ EGDMA	903	1.055	0.095	0.764	17	63480	22.9
DMAEMA1PEG2	1181	1.080	0.074	0.813	21	50660	22.1
DMAEMA5PEG2	1301	1.057	0.067	0.808	13	77460	28.1
DMAEMA10PEG2	1920	1.061	0.046	0.817	11	82630	32.5
DMAEMA20PEG2	2563	1.052	0.037	0.829	9	94630	37.2
DMAEMA1PEG10	1290	1.053	0.068	0.802	19	52800	23.1
DMAEMA5PEG10	2370	1.059	0.038	0.787	10	83770	34.7
DMAEMA10PEG10	2506	1.051	0.036	0.847	9	94985	37.6
DMAEMA20PEG10	2507	1.053	0.036	0.874	8	109100	40.3
DMAEMA1PEG20	1997	1.052	0.045	0.787	12	72950	30.8
DMAEMA5PEG20	1350	1.053	0.064	0.792	18	54310	23.9
DMAEMA10PEG20	1539	1.057	0.054	0.837	19	50740	24.3
DMAEMA20PEG20	2452	1.053	0.043	0.863	9	101510	36.8

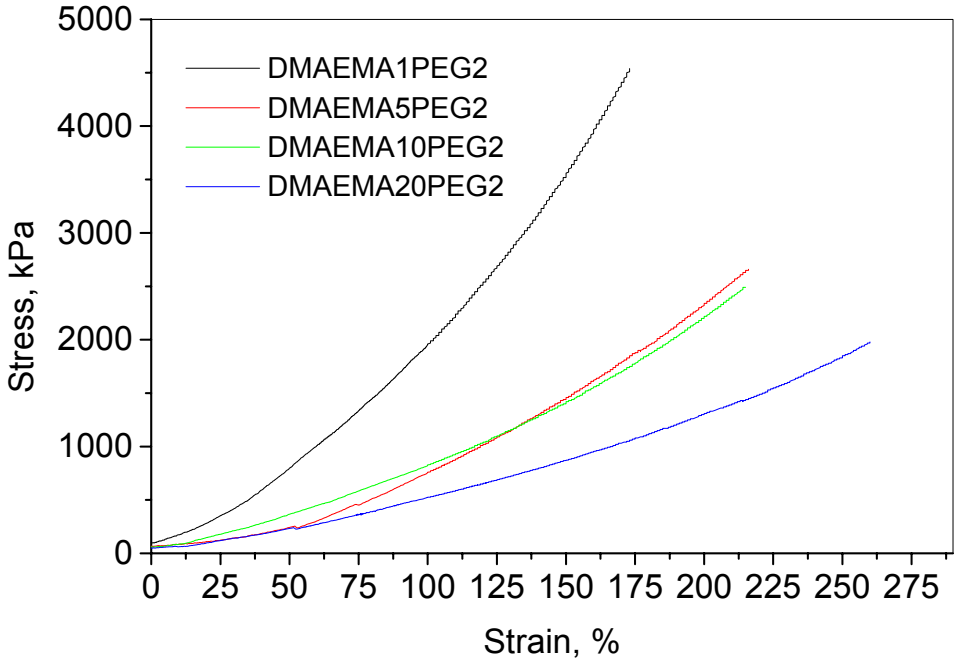


Fig. 6.15. Stress versus strain curves of DMAEMAXPEG2 hydrogels. (The amount of PEG in the initial mixture; X = 1%, 5 %, 10% and 20%

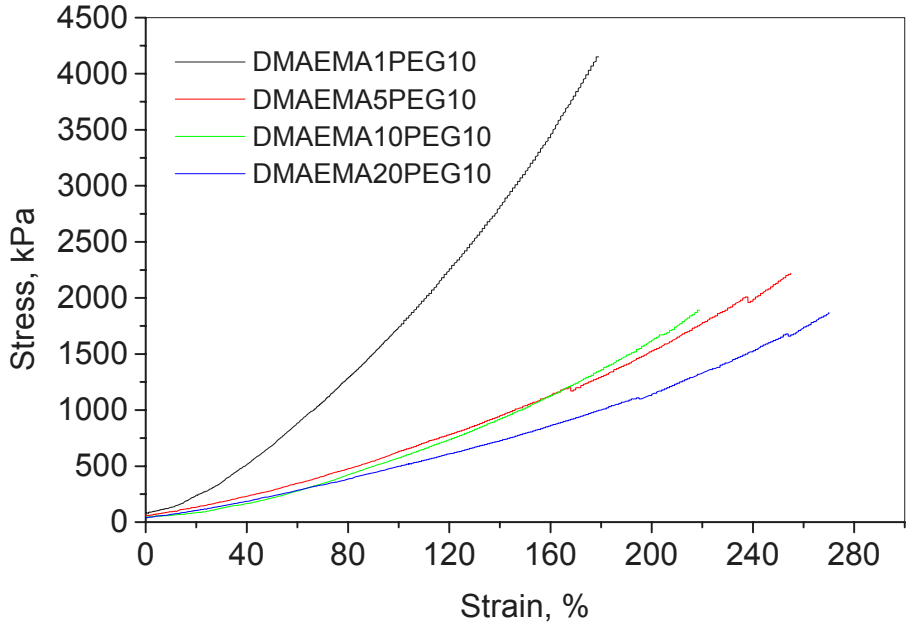


Fig. 6.16. Stress versus strain curves of DMAEMAXPEG10 hydrogels. (The amount of PEG in the initial mixture; X = 1%, 5 %, 10% and 20%

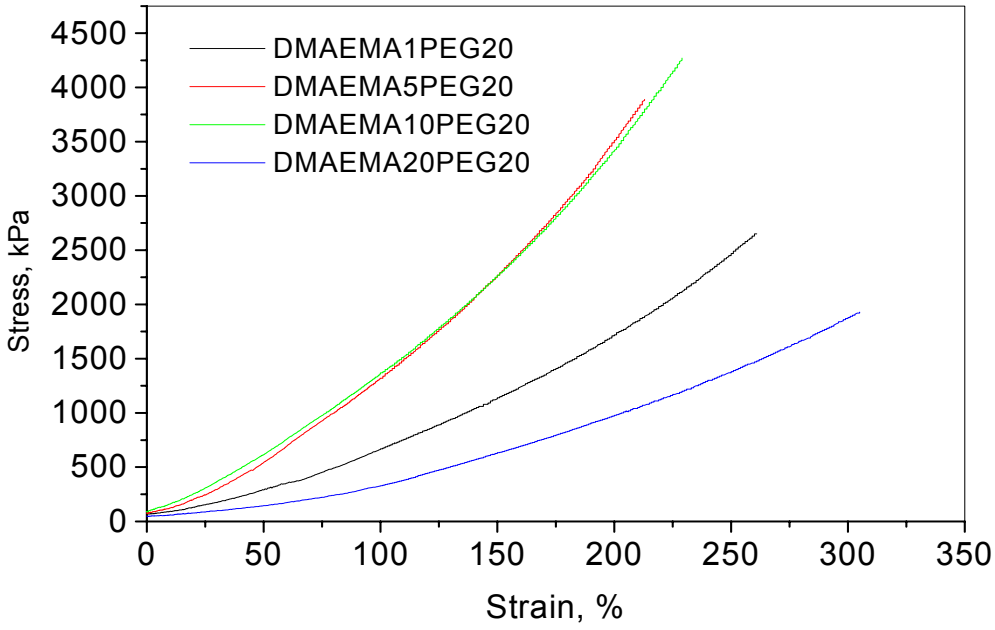


Fig. 6.17. Stress versus strain curves of DMAEMAXPEG20 hydrogels. (The amount of PEG in the initial mixture; X = 1%, 5 %, 10% and 20%

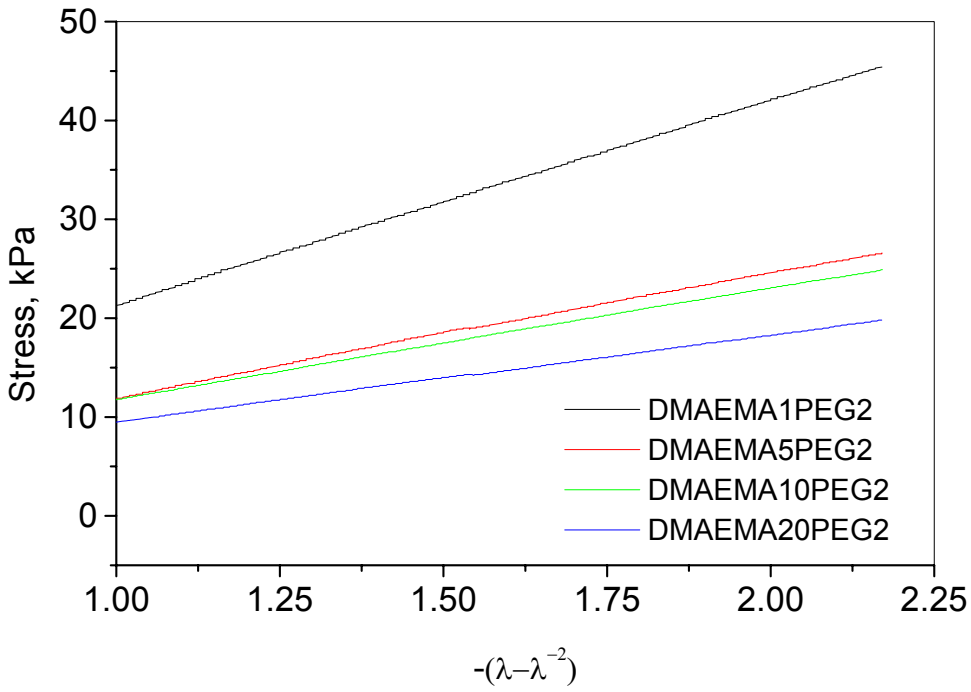


Fig 6.18. Stress versus $-(\lambda-\lambda^{-2})$ curves of DMAEMAXPEG2 hydrogels. (The amount of PEG in the initial mixture; X = 1%, %5, 10% and 20%

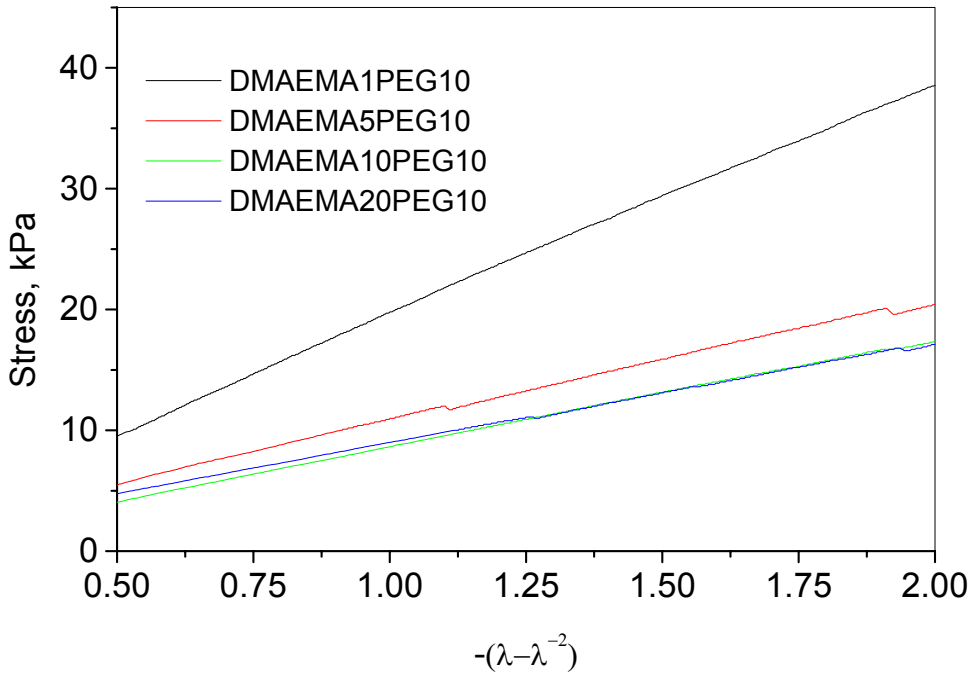


Fig. 6.19. Stress versus -(λ-λ^{-2}) curves of DMAEMAXPEG10 hydrogels. (The amount of PEG in the initial mixture; X = 1%, %5, 10% and 20%

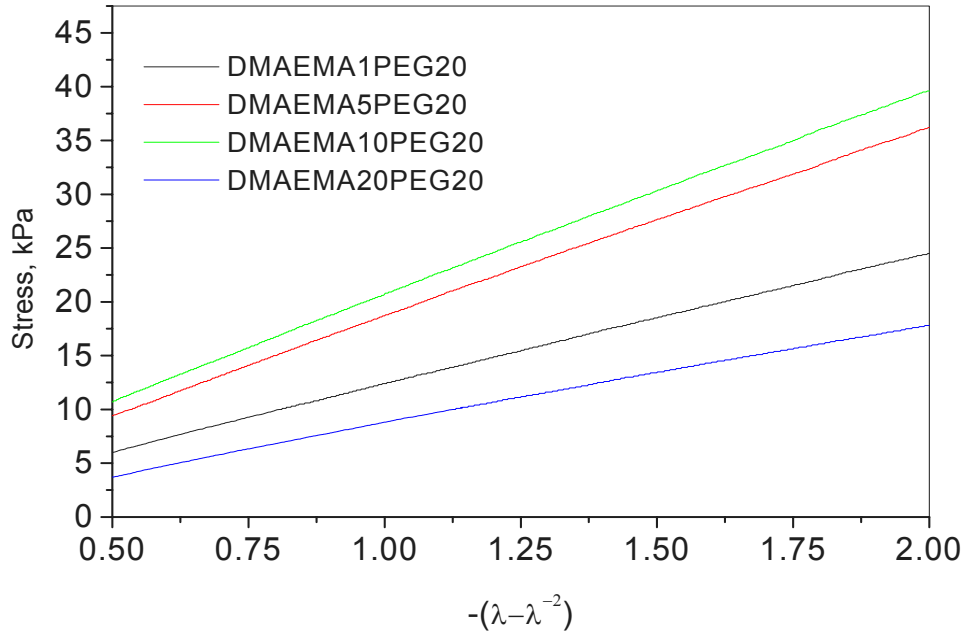


Fig. 6.20. Stress versus -(λ-λ^{-2}) curves of DMAEMAXPEG20 hydrogels. (The amount of PEG in the initial mixture; X = 1%, %5, 10% and 20%

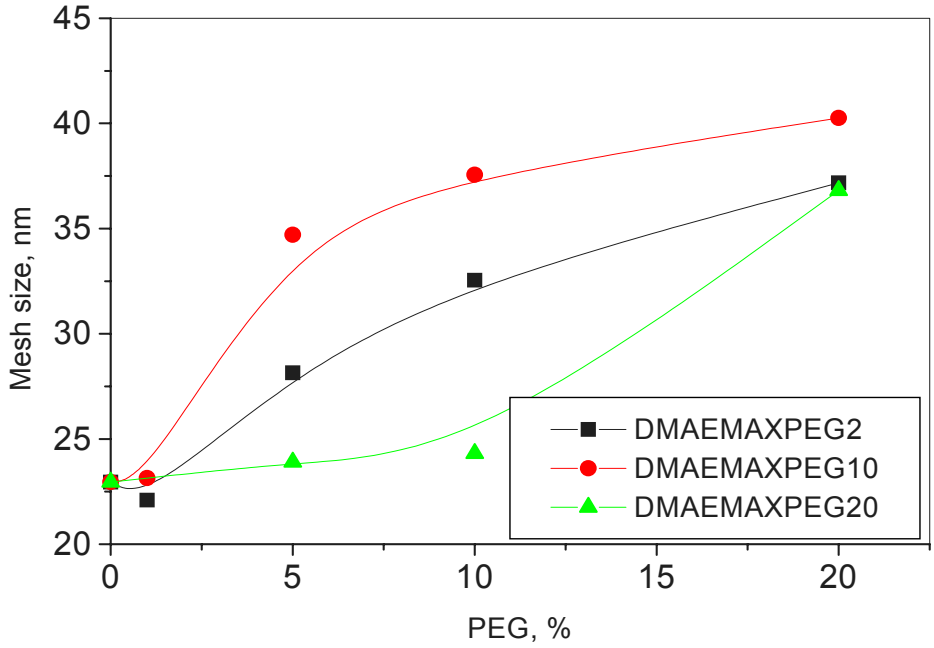


Fig. 6.21. Effect of PEG content in the initial mixture on the mesh size of PDMAEMA hydrogels

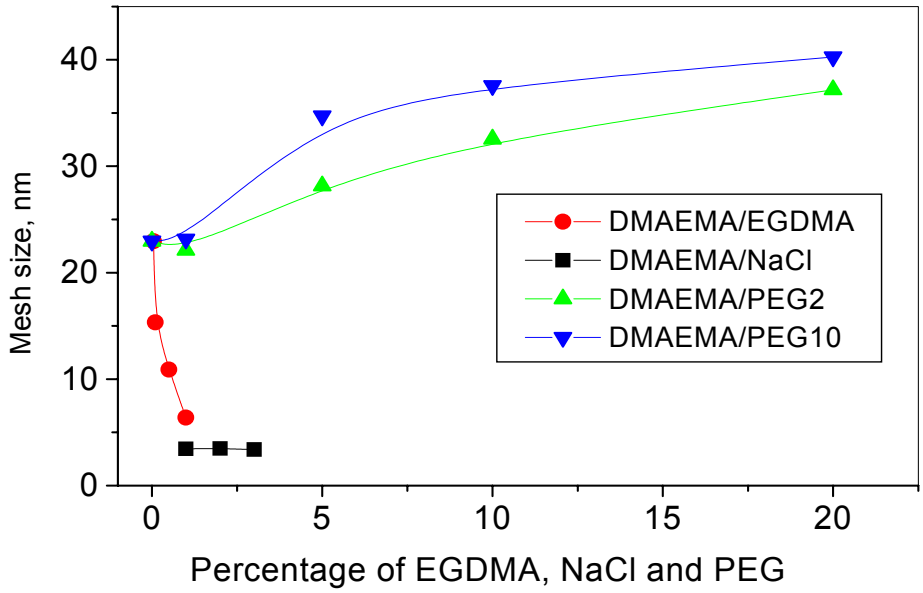


Fig. 6.22. The effect of EGDMA, NaCl and PEG in the initial mixture on the mesh size of PDMAEMA hydrogels.

6.7. Swelling of P(DMAEMA) Hydrogels in Buffer Solutions

In order to follow the pH response of the PDMAEMA hydrogels prepared in the presence of PEG, dry samples are allowed to swell to equilibrium in phosphate buffer of varying pH at fixed ionic strength (I = 0.01) and temperature (25ºC). Fig. 6.23 - 6.25 show the changes in the equilibrium degree of swelling of all PDMAEMA hydrogels with changing pH value. The equilibrium degree of swelling (EDS) was defined as Q= 1/ υ_{2m}.

Consistent with poly-electrolytic systems, swelling of these gels are strongly dependent on pH (Şen, M. and Güven O., 2001, Güven O. and Şen M., 1998). A decrease in the pH from 8 to 2 caused a significant increase in the equilibrium volume swelling ratio of hydrogels. Among all PEG contents maximum extent of swelling was reached at pH 3, this being due to the complete protonization of amine groups of PDMAEMA at this pH value.

It has been found that, cross-linked polymer gels based on n-alkyl esters of methacrylic acid, including ethyl methacrylate (EMA) polymerized with N,N – dimethylamino ethyl methacrylate (DMAEMA) display aqueous equilibrium swelling properties that depend strongly on the pH and ion composition of the solution. (Siegel and Firestone, 1988). These gels generally undergo a sharp pH-induced swelling transition from a collapsed, hydrophobic state to a swollen ionized hydrophilic state as solution pH is reduced into the acidic range. Such swelling behavior has been attributed to alterations in the internal osmotic balance of the gel brought by changes in the ionic composition of the external solution. The inherent hydrophobicity of these gels, which dominates at high pH and favors the exclusion of water, is opposed by the development of an internal ion osmotic pressure at lower pH, as a result of protonization of the gel amine groups, which induces water imbibition and gel swelling. Thus, their hydrophobicity was dominant at pH values above 6.6 and as the pH was lowered, the tertiary amine side chains on the N,N-dimethylamino ethyl methacrylate became protonated causing an increase in the charge density of the network. This resulted in electrostatic repulsion between these groups and swelling of the network ensured(Siegel and Firestone,1988)

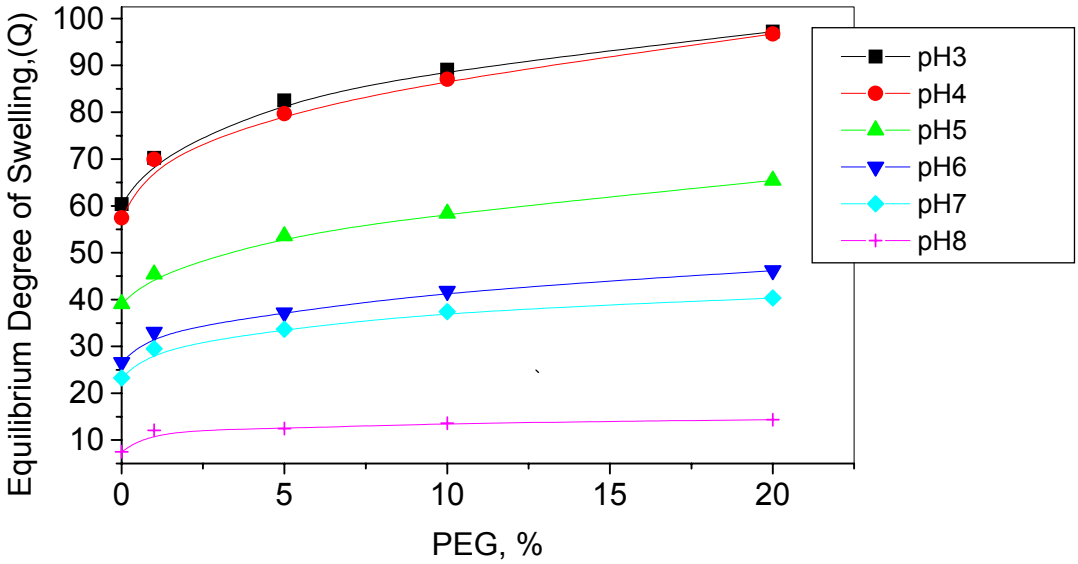


Fig. 6.23. The effect of pH and the amount of PEG2000 in the initial mixture on the EDS values of PDMAEMA hydrogels.

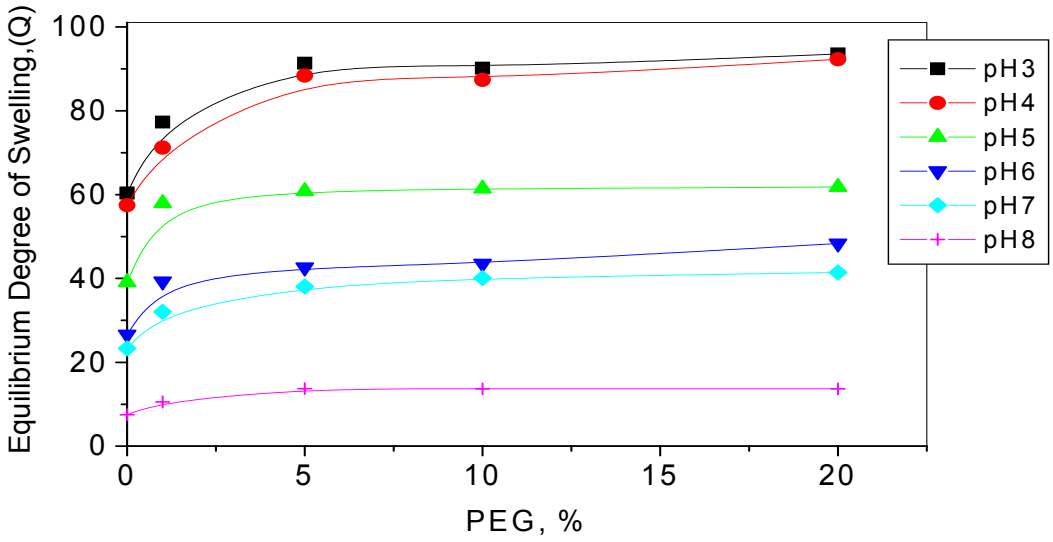


Fig. 6.24. The effect of pH and the amount of PEG10000 in the initial mixture on the EDS values of PDMAEMA hydrogels.

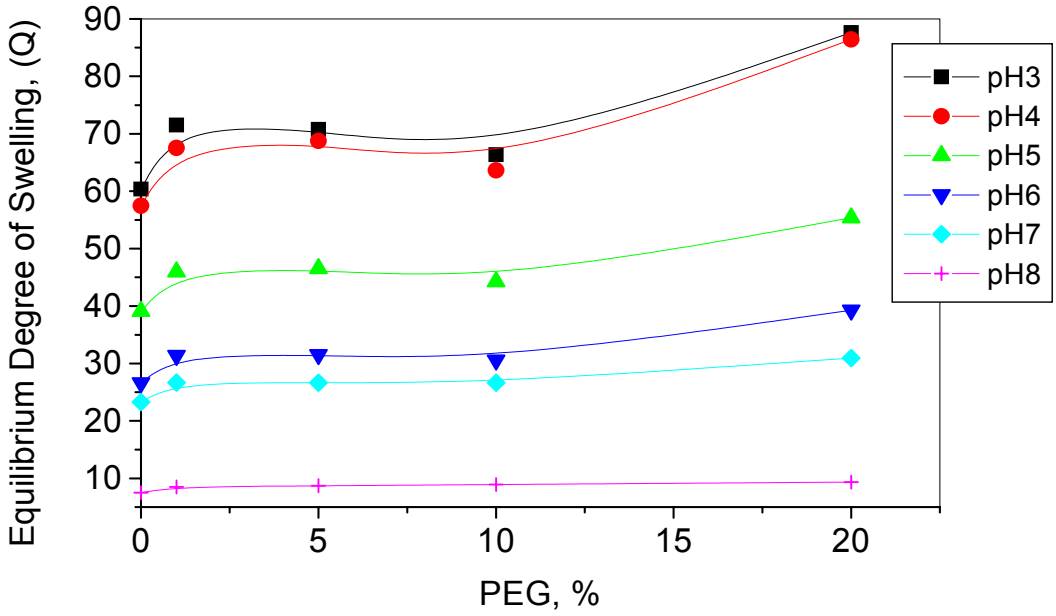


Fig. 6.25. The effect of pH and the amount of PEG20000 in the initial mixture on the EDS values of PDMAEMA hydrogels.

In order to investigate the effect of molecular weight of PEG used in the preparation on swelling behaviour of PDMAEMA hydrogels, the molecular weight of PEG was plotted versus equilibrium degree of swelling(Q). As can be seen from Fig. 6.26 - 6.29, equilibrium degree of swelling (Q) increases with increasing molecular weight of PEG until 10000 molecular weight. It was found that the addition of PEG over the 10000 molecular weight didn't change or slightly decreased the equilibrium degree of swelling. When 1 and 5 % PEG used in the initial mixture maximum extent of swelling was obtained with 10000 molecular weight having PEG. However, for the hydrogels containing 10% and over 10% PEG maximum swelling was reached at 2000 molecular weight .

These results show that, mesh size of hydrogels can be controlled by changing the molecular weight and concentration of PEG.

In order to investigate the effect of pH on the mesh size, the mesh size values (ξ) of hydrogels were calculated by using Eq. 6.5 and given in Fig. 6.30 - 6.33. As can be seen from the figures, the mesh size of hydrogels were affected from pH and increased approximately two fold with a change of pH from 8 to 3 for all PDMAEMA hydrogels.

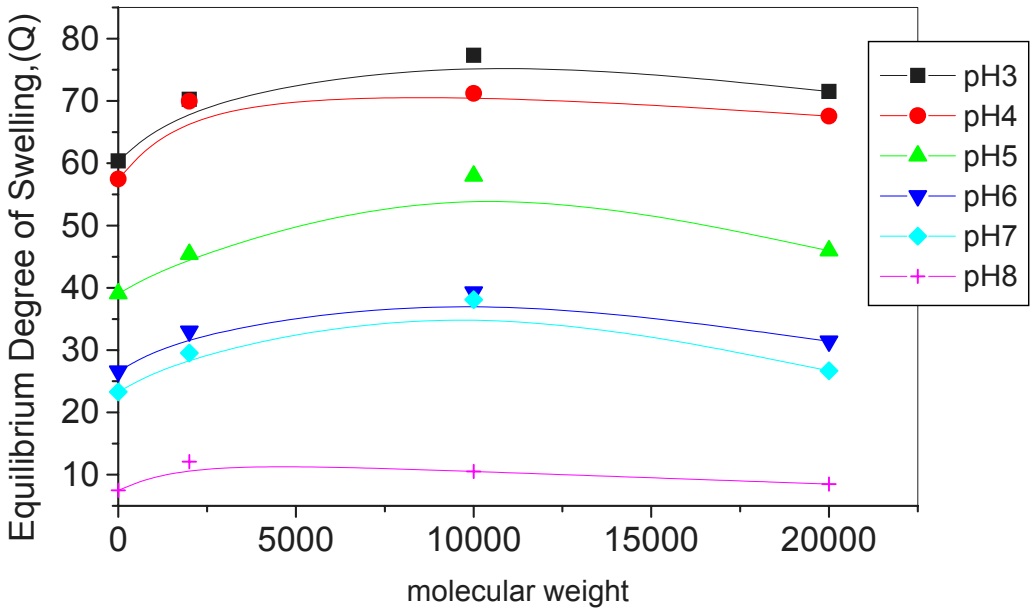


Fig. 6.26. Variation of EDS values of PDMAEMA hydrogels with the pH of the swelling solution and the molecular weight of PEG. The amount of PEG in the initial mixture is 1%.

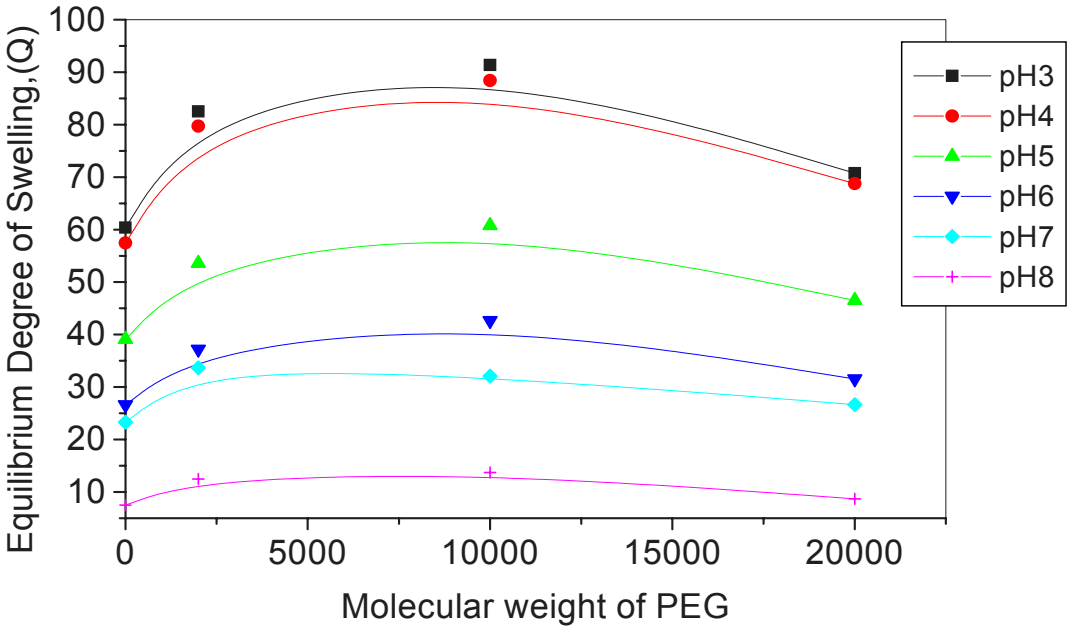


Fig. 6.27. Variation of EDS values of PDMAEMA hydrogels with the pH of the swelling solution and the molecular weight of PEG. The amount of PEG in the initial mixture is 5 %.

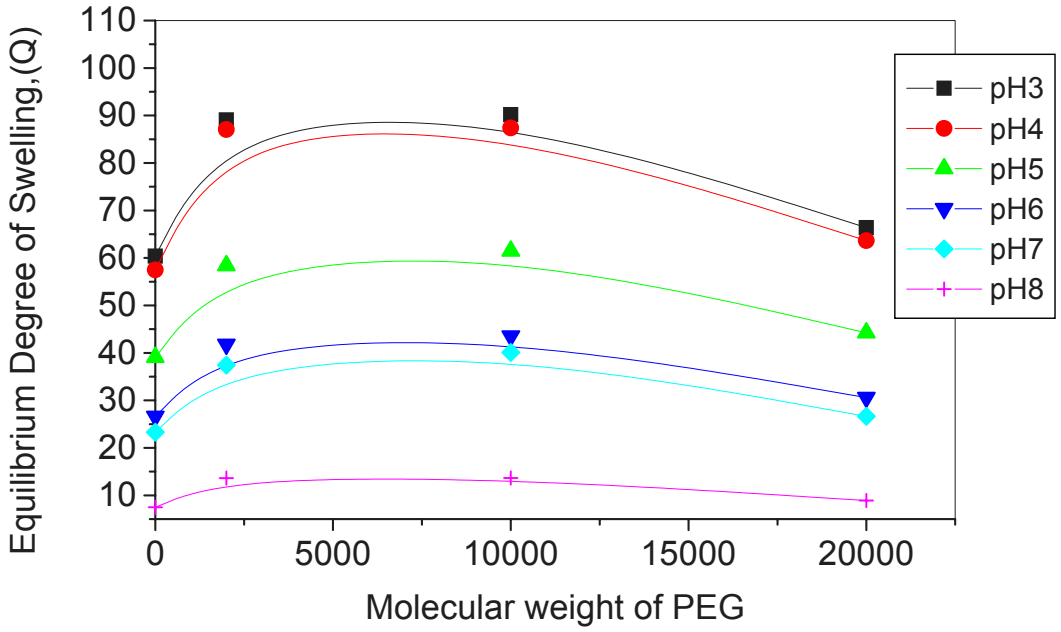


Fig. 6.28. Variation of EDS values of PDMAEMA hydrogels with the pH of the swelling solution and the molecular weight of PEG. The amount of PEG in the initial mixture is 10 %.

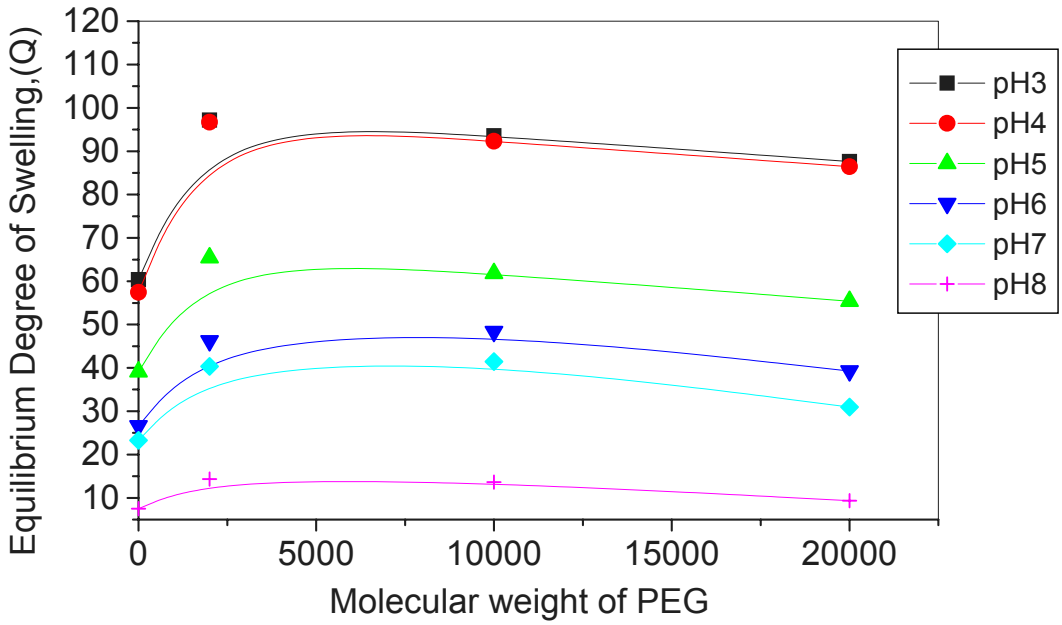


Fig. 6.29. Variation of EDS values of PDMAEMA hydrogels with the pH of the swelling solution and the molecular weight of PEG. The amount of PEG in the initial mixture is 20 %.

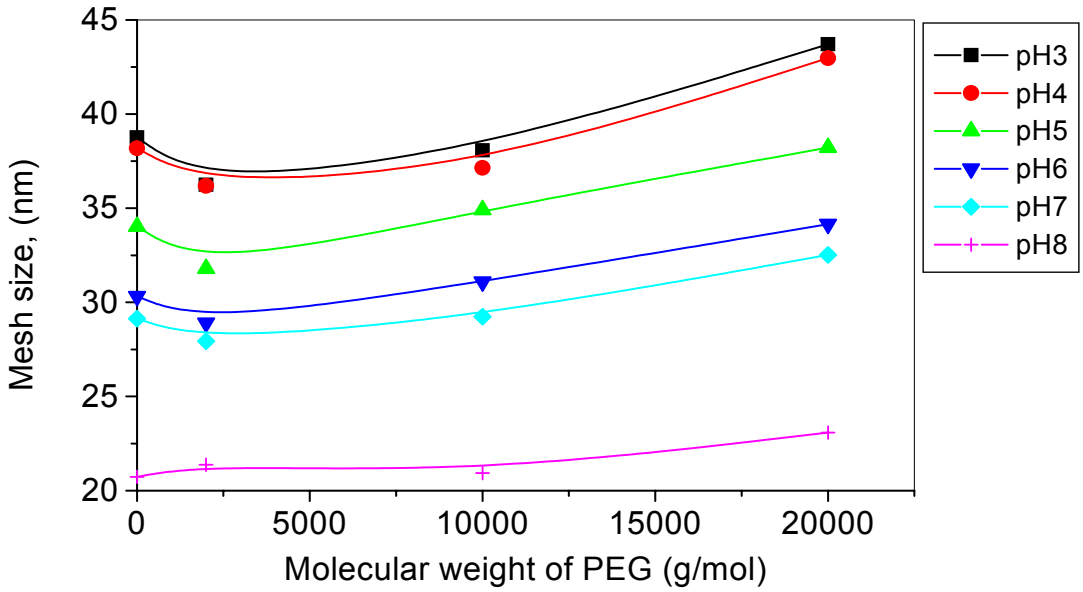


Fig. 6.30. Variation of the mesh size values of PDMAEMA hydrogels with the pH of the swelling solution and the molecular weight of PEG. The amount of PEG in the initial mixture is 1 %.

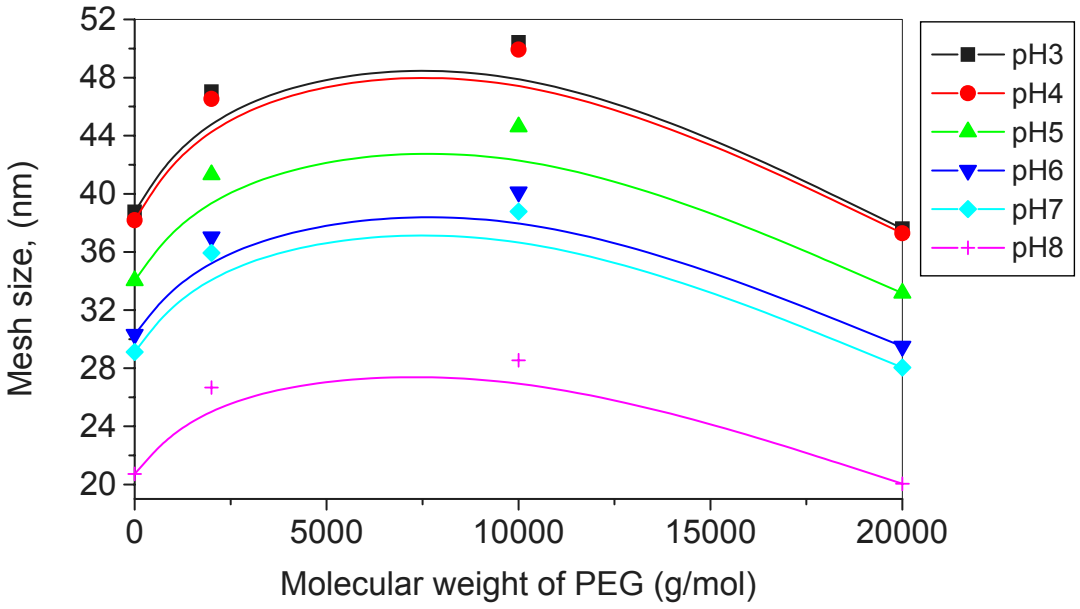


Fig. 6.31. Variation of the mesh size values of PDMAEMA hydrogels with the pH of the swelling solution and the molecular weight of PEG. The amount of PEG in the initial mixture is 5 %.

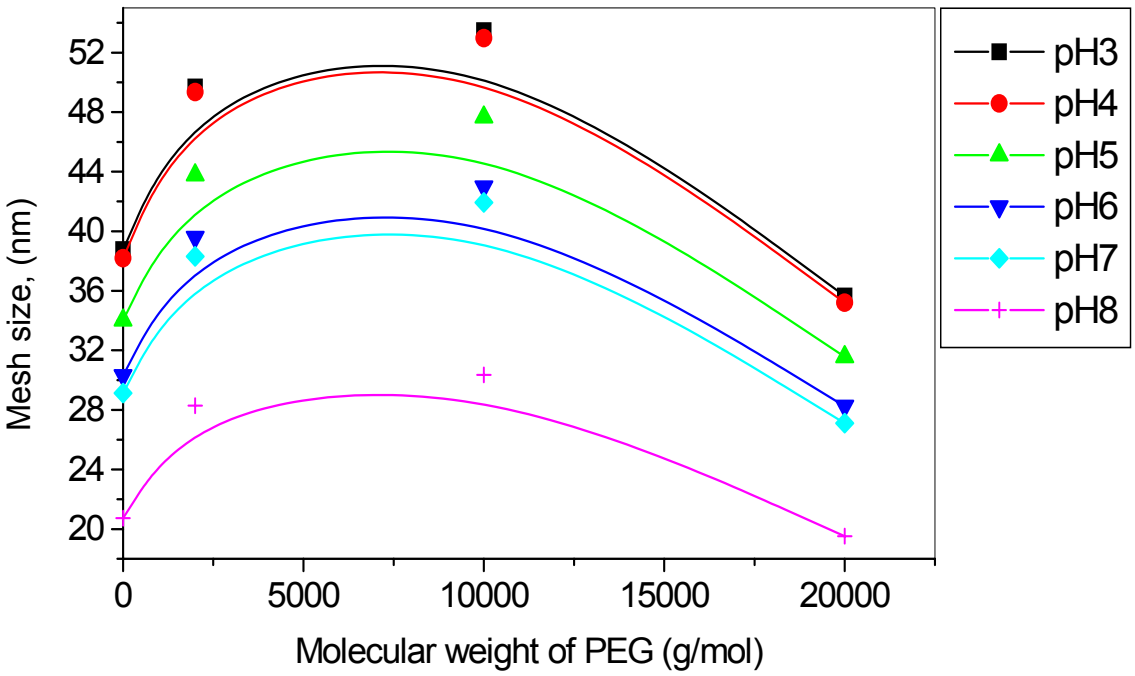


Fig. 6.32. Variation of the mesh size values of PDMAEMA hydrogels with the pH of the swelling solution and the molecular weight of PEG. The amount of PEG in the initial mixture is 10 %.

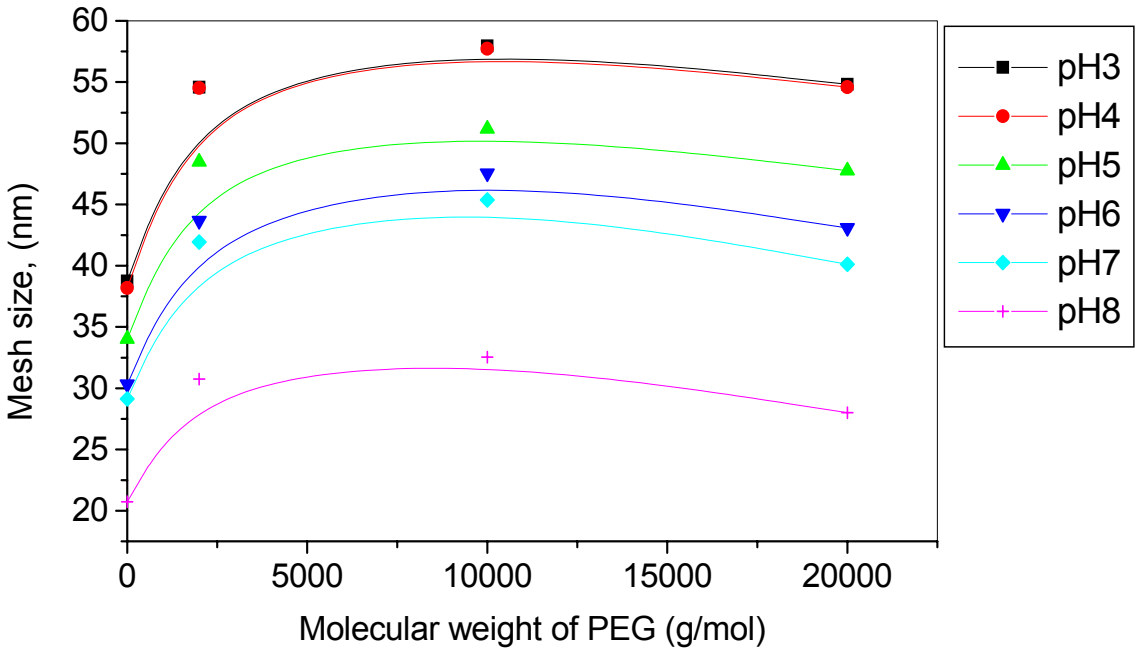


Fig. 6.33. Variation of the mesh size values of PDMAEMA hydrogels with the pH of the swelling solution and the molecular weight of PEG. The amount of PEG in the initial mixture is 20 %.

6.8. SEM Studies

The effect of pH and the amount of PEG2000 on the pore structure of hydrogels was monitored by using a scanning electron microscope. SEM pictures of DMAEMA/0.05EGDMA and DMAEMA1PEG20, DMAEMA5PEG20, DMAEMA10 PEG20 and DMAEMA20PEG20 hydrogel systems were given in Fig. 6.34. - 6.37. The magnifications in Fig 6. 34 and Fig. 6.36 is 35 and Fig. 6.35 and Fig. 6. 37 is 200. Fig. 6. 34- 6.35 and Fig. 6.36 -6.37 represent the SEM pictures of hydrogels swelled in pH 3 and 7 respectively. As can be seen from figures, pore structure of the hydrogels are homogeneous and pores are opened with the decrease of pH. Pictures also indicate that the effect of porogen PEG2000 content on the pore size structure of the hydrogel systems can not easily be monitored at low magnifications at pH 7 and at high magnifications at pH 3. Pictures in Fig. 6.37 clearly show that increase of PEG2000 content in the initial mixture increase the pore size of hydrogel system.

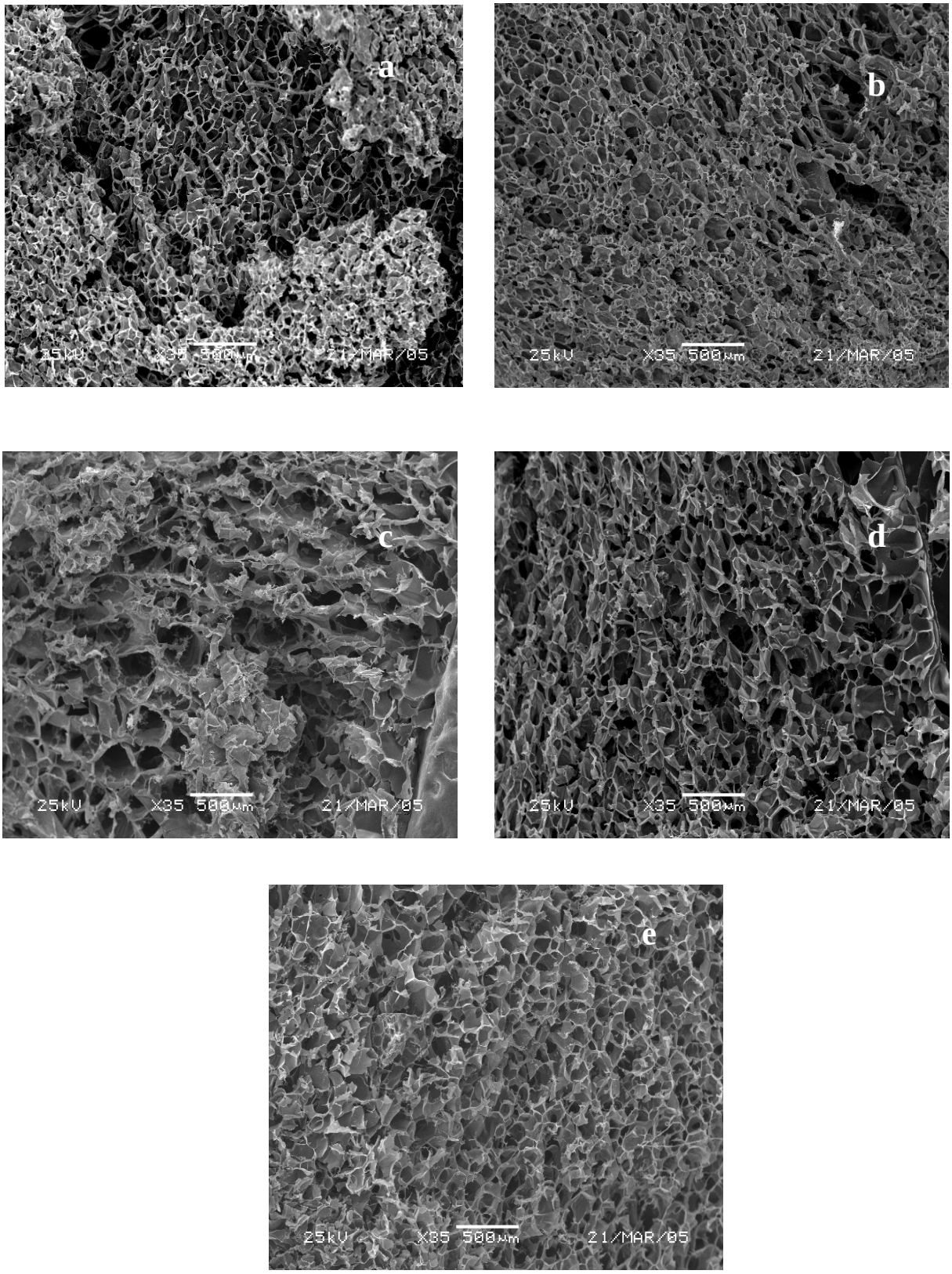


Fig. 6. 34. SEM pictures of a) DMAEMA/0.05EGDMA, b) DMAEMA1PEG2 c) DMAEMA5PEG2 d)) DMAEMA10PEG2 e)) DMAEMA20PEG2 hydrogel systems swelled at pH 3. The magnification is 35

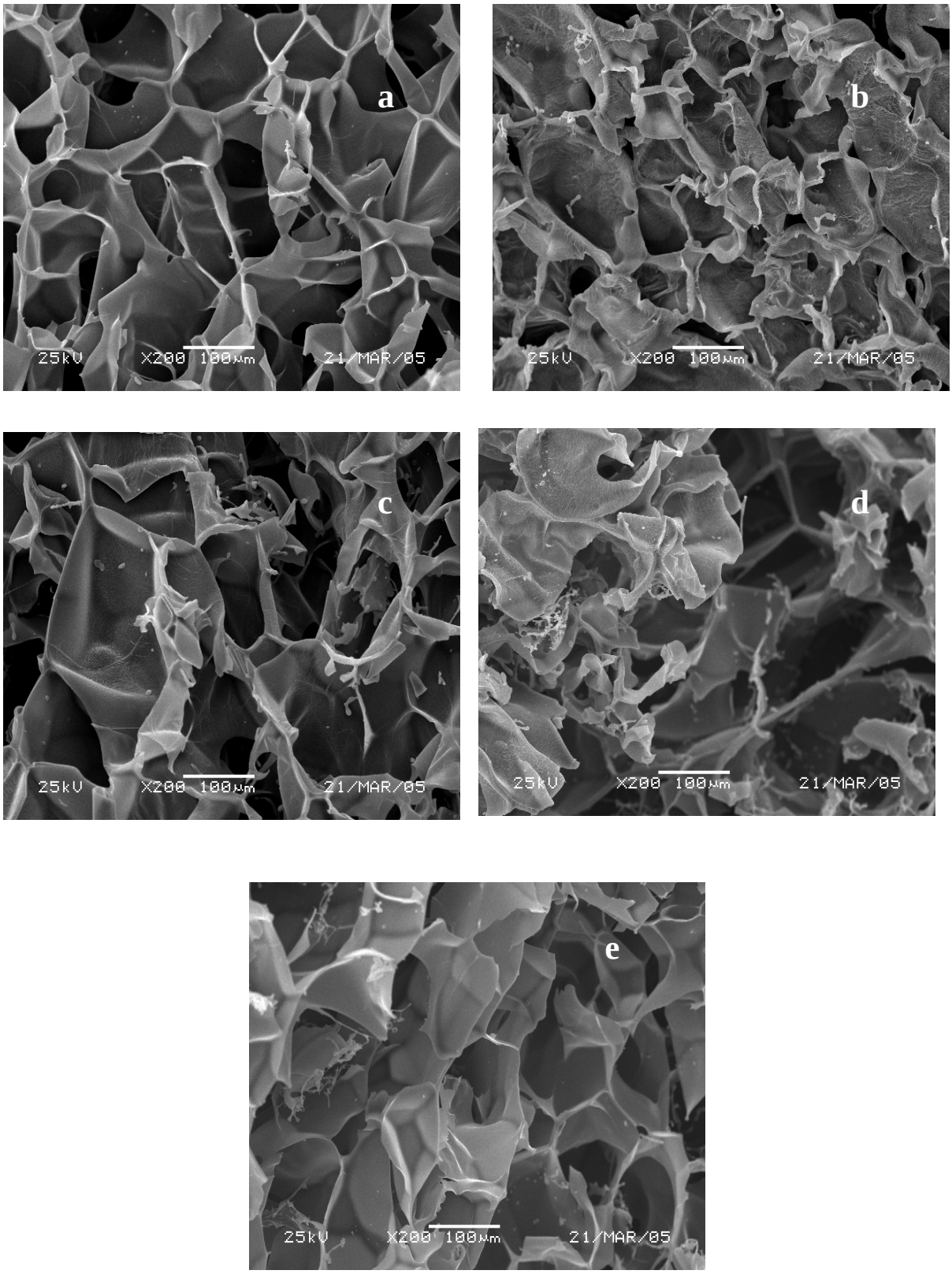


Fig. 6. 35. SEM pictures of a) DMAEMA/0.05EGDMA, b) DMAEMA1PEG2 c) DMAEMA5PEG2 d)) DMAEMA10PEG2 e)) DMAEMA20PEG2 hydrogel systems swelled at pH 3. The magnification is 200

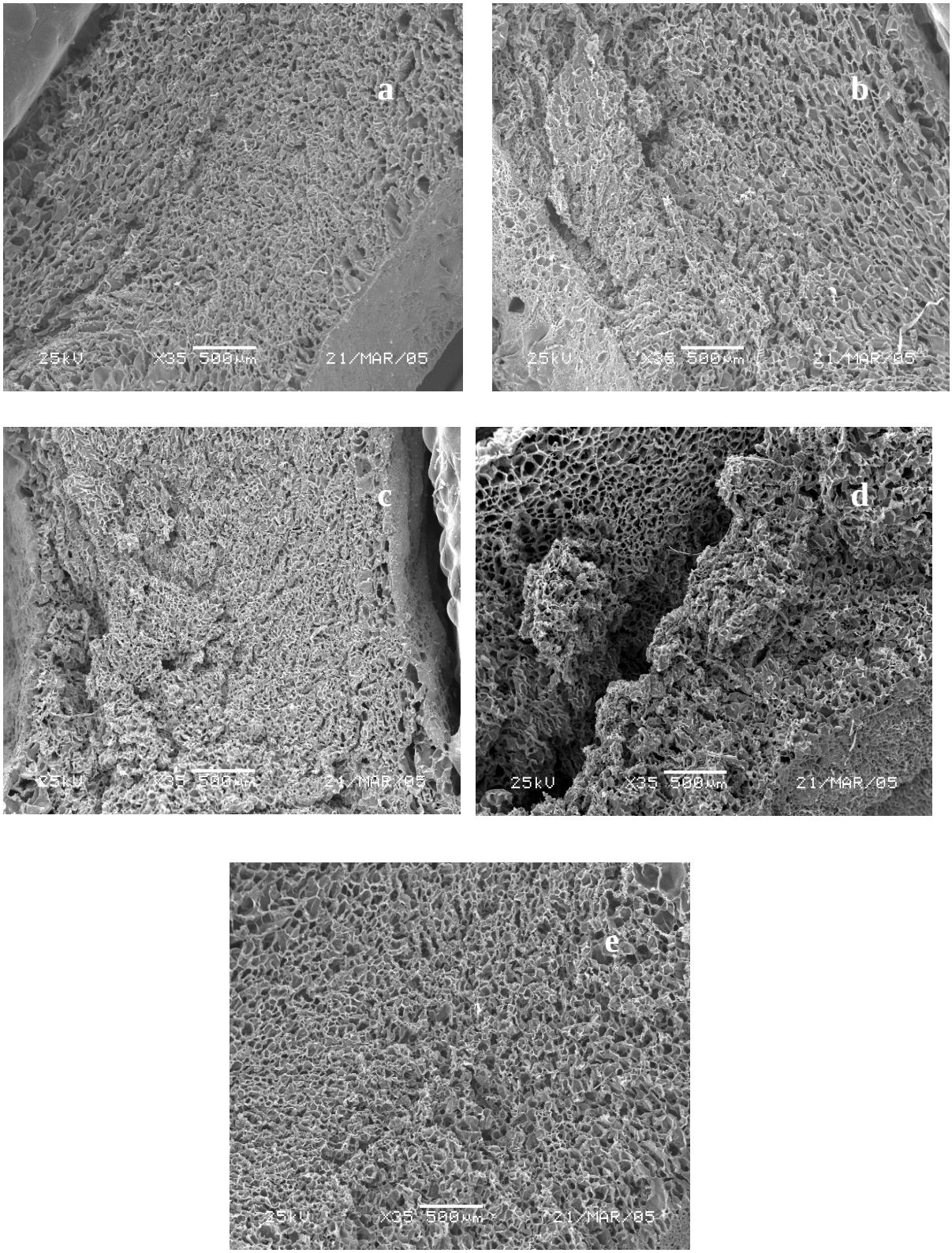


Fig. 6. 36. SEM pictures of a) DMAEMA/0.05EGDMA, b) DMAEMA1PEG2 c) DMAEMA5PEG2 d)) DMAEMA10PEG2 e)) DMAEMA20PEG2 hydrogel systems swelled at pH 7. The magnification is 35

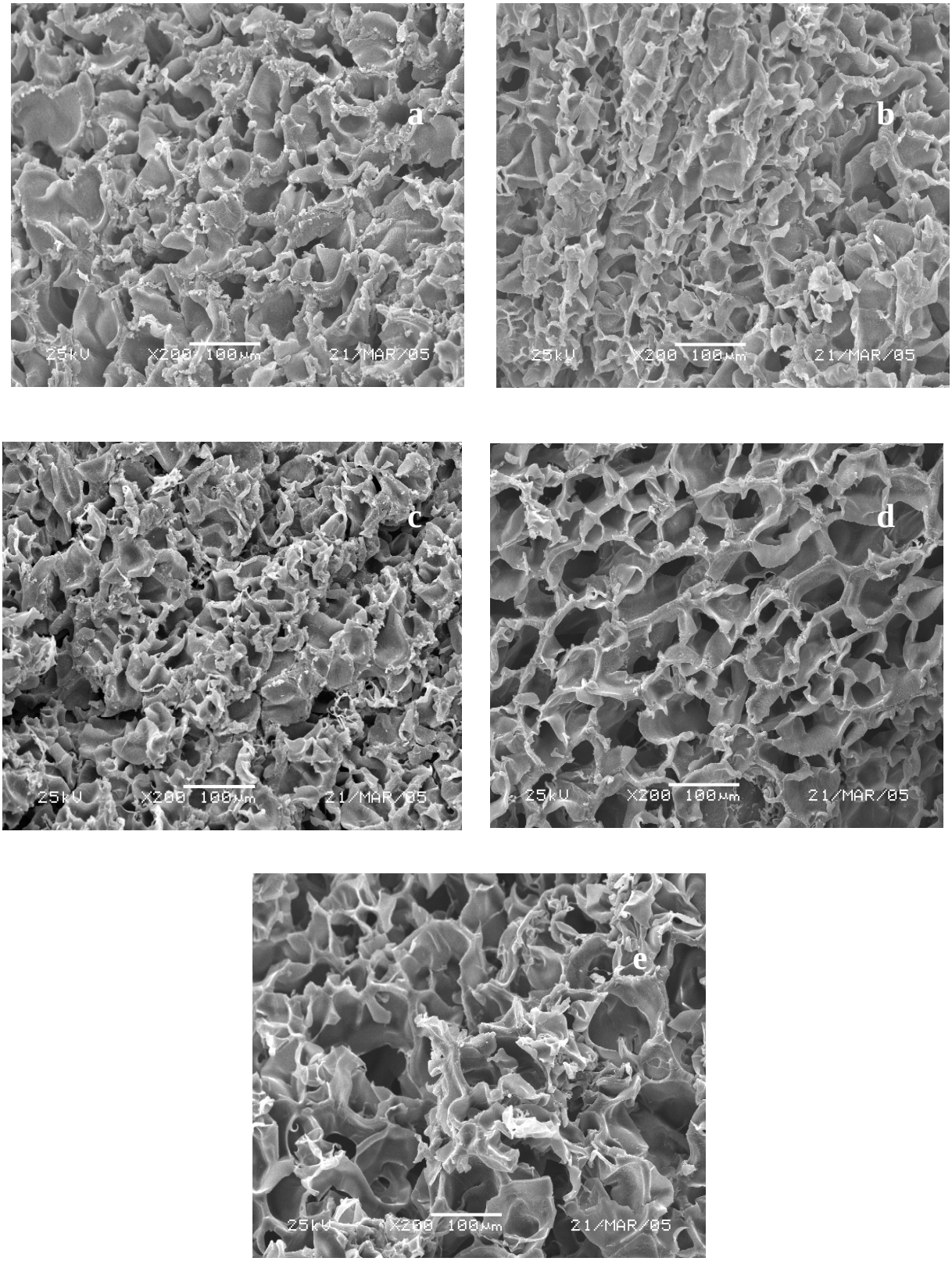


Fig. 6. 37. SEM pictures of a) DMAEMA/0.05EGDMA, b) DMAEMA1PEG2 c) DMAEMA5PEG2 d)) DMAEMA10PEG2 e)) DMAEMA20PEG2 hydrogel systems swelled at pH 7. The magnification is 200

7. FINDINGS

- The aqueous solution of DMAEMA monomer shows a very low tendency to cross-link when irradiated with gamma rays at low dose rates.
- The percentage gelation of DMAEMA increases from 10 % to 97 % by the addition of only 0.1 % EGDMA in the aqueous solution of DMAEMA and increased slightly with the increasing of the cross-linking agent content.
- The aqueous solutions of N,N-Dimethylamino ethyl methacrylate (DMAEMA), were irradiated with γ - rays to 4 kGy in the presence of porogen NaCl and PEG in order to improve the mesh size of PDMAEMA hydrogels
- Monomer-gel conversion of DMAEMA monomer did not change with the addition of NaCl in the initial mixture.
- PEG affected the % gelation of DMAEMA and gelation was decreased with the decrease of molecular weight of the PEG and with the increasing PEG content in the initial mixture.
- Molecular weight between cross-links of hydrogels decreased with increasing cross-linking agent EGDMA, and adding 1 M NaCl solution into the initial mixture.
- The network mesh size, ξ, was calculated. The mesh size in P(DMAEMA/ EGDMA) hydrogels decreased from 22.6 to 6.4 nm with increasing cross-linking agent content in the hydrogel structure from 0.05 to 1.0 % and decreased from 10.9 to 3.4 nm with increasing of NaCl concentration from 0 to 1 M.
- Molecular weight between cross-links of hydrogels increased with poly (ethylene glycol) PEG, used in the initial mixture.
- Addition of PEG2000 and PEG10000 in the initial mixture the mesh size has been increased approximately two fold.
- The mesh size in PDMAEMA hydrogels prepared in the presence of PEG increased with increasing the amount of PEG in the initial mixture from 1 to 20%.
- Mechanical properties of these hydrogels were investigated with applying compression test and Elastic Modulus values of hydrogels were calculated by using elastic deformation.

- pH swelling experiments were carried out pH 3-8 in phosphate buffer solutions. For all prepared hydrogels the equilibrium degree of swelling (EDS), Q, valued increased with decreasing pH.
- Effect of molecular weight of PEG and percentage of PEG, on swelling, were investigated. Equilibrium Degree of Swelling (Q) increases with increasing molecular weight of PEG until 10000 molecular weight. Addition of PEG over the 10000 molecular weight in the initial mixture equilibrium degree of swelling (Q) didn't change or slightly decreased.
- Mesh size of hydrogels were affected from pH and increased approximately two fold when the pH changed from 8 to 3.
- Pore structure of hydrogels was monitored by using scanning electron microscope and it was found that pore structure of hydrogels are very homogeneous and pores open with the decrease of pH and increase of PEG2000 content in the initial mixture.
- All these results show that the pore structure of PDMAEMA hydrogels can be controlled by changing the amount of PEG in the initial mixture and the molecular weight of it.
- PDMAEMA hydrogels prepared in this thesis in the presence of PEG can be assume macroporous materials at low pH values. On the other hand same polymer also can be called as microporous hydrogel at high pH values.

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