CHAPTER I
INTRODUCTION AND LITERATURE REVIEW

1.1. Effect of Ionizing Radiation on Polymeric Materials

(Pengfei, 2005) reported that the radiation technologies applying gamma sources and electron accelerators for material processing are well-established processes. The technologies to be developed besides environmental applications could be nanomaterials, structure engineering materials and natural polymers processing.

1.1.1. Sources of Ionizing Radiation

(Wilson, 1974) reported that the ionizing radiation covers different types of radiation, such as electromagnetic waves, X-rays and γ-rays from radioisotopes (cobalt-60 and cesium-137). Also β-rays and electron beams generated by electron accelerators. Heavy particle radiations (e.g. alpha, accelerated deuteron and heavier ions) and neutron beams may be used for special purposes. It can be easily seen that there are generally undetectable differences in the effects produced by electrons and gamma rays at equal doses. Fast moving electrons lose their energy through electrostatic interaction with the electrons of irradiated medium. If energy transferred from the incident particles is higher than the binding energy of the electrons in the molecule, an electron may be ejected leaving behind a positively charged "ionized" molecule. If the amount of energy transferred to the molecule is less than its lowest ionization potential, electronic excitation may occurring giving rise to an

excited state, which may or may not dissociate further into free radicals.

The two most common radiation types in industrial use are gamma and electron beam. The gamma facilities are mainly cobalt-60 ***(Chapiro, 1993).*** The advantages of gamma radiation over other types include the fact that gamma rays are very penetrating. The technology is extremely simple, so there is low downtime for a gamma source. In addition, it is not sensitive to electricity prices. Gamma sources are most commonly used today for radiation sterilization of disposable plastic medical items ***(Halls, 1991).***

Electron beam machines play a significant role in the processing of polymeric materials; a number of different machine designs and different energies are available. Industrial electron beam accelerators with energies in the 150–300 MeV range are used in applications where low penetration is needed, such as curing of surface coatings ***(Begam et al, 2003)***. Accelerators operating in the 1.5 MeV range are used where more penetration is needed, as in the cross-linking of cable insulation. High-energy commercial electron beams, operating in the 10 MeV range, are used for applications such as sterilization of boxes filled with disposable medical devices ***(Descamps, 1995).*** Electron beam machines have a high-dose rate and therefore short processing times. While they have limited penetration compared with gamma, they conversely have good utilization of energy due to the following aspects: (1) All can be absorbed by the sample being irradiated. (2) Can be switched off when it is not in use. (3) They contain no radioactive isotope; this provides an advantage from a public acceptance standpoint. (4) No

radioactive material is disposed off when the facility is decommissioned.

Ion beams are being used to create new technology in polymer processing ***(Saha et al, 2000 and Virk, 2002).*** Whereas they have been extensively applied in commercial application for ion implantation in the production of semiconductor devices, and have been applied for surface hardening of metals, they are just beginning to be adapted for commercial use with macromolecular materials ***(Singh, 2004).*** A great variety of different ion-beam machines are in existence, having widely varying energies, and operating in both continuous and pulsed mode ***(Phukan et al, 2002 , Senna and Abd Hamide, 2002).*** Ions are of most interest for treatment of polymer surfaces and thin films because they have extremely low penetration depths. Many different ions have been employed for irradiating polymers, ranging from hydrogen and helium ions, up to ions of heavy elements ***(Cataldo et al, 2004).***

1.1.2. Interaction of Radiation with Polymeric Materials

(Bhattacharya, 2000) reported that radiation technology is preferred over the other conventional energy resources due to some reasons, e.g. large reactions as well as product quality can be controlled, saving energy as well as resources, clean processes, automation and saving of human resources etc. The irradiation of polymers can be applied in various sectors. The main applications are for modification of polymer materials through radiation crosslinking, degradation and grafting.

When the radiation from a gamma ray, electron beam or X-ray source interacts with a polymer material, its energy is absorbed by the polymer material and active species such as radicals are produced, thereby initiating various chemical reactions ***(Singh et al, 2004)***. The mechanism by which the radiation transfers the energy to the matter depends essentially upon the type of the radiation. The overall effects of the three types of ionizing radiation are the creation of ionization and excitation, i.e. the production of ions and excited states. These species subsequently react in a number of ways, the result of which is the production of free radicals. The formed free radicals can react in a variety of ways, either uimolecularly or bimolecularly, with other radicals or with stable molecules to give stable products. The effect of ionizing radiation on high polymers may bring about different types of reactions. Two reaction processes occur when electromagnetic radiation passes through matter; it may interact either with the atomic nucleus or with orbital electrons. In the case of polymeric materials, reactions with orbital electrons are more frequent of the macromolecules, giving rise to a positive ion.

$$-CH_2-R \quad ^{^{^{\rightarrow}}} \quad -^{*}CH_2-R + e^{-} \qquad (1)$$

When the ionized molecules are discharged by the thermal electrons, highly excited molecules are formed.

$$-^{*}CH_2-R + e^{-} \rightarrow -^{*}CH_2-R \qquad (2)$$

These excited molecules are decomposed into free radicals

$$-^{*}CH_2-R \rightarrow -^{\bullet}CH-R + {}^{\bullet}H \qquad (3)$$

Thus, the primary effect of radiation on the polymer molecule is the formation of free radicals and the loss of atomic hydrogen. The free radicals can undergo a variety of reactions of four types as follows:

(1) Abstraction

The hydrogen atom formed in reaction **(3)** may abstract a hydrogen atom from another polymer molecule, forming molecular hydrogen and a new radical is formed.

$$-CH_2-R + {}^{\bullet}H \rightarrow -{}^{\bullet}CH-R + H_2 \qquad (4)$$

(2) Recombination

The recombination of free radicals is a process converse to decomposition of excited molecules and may lead to the formation of crosslinking.

$$\begin{array}{l} R-{}^{\bullet}CH-R \\ \qquad + \quad \rightarrow \\ R-{}^{\bullet}CH-R \end{array} \qquad \begin{array}{l} R-CH-R \\ \quad | \\ R-CH-R \end{array} \qquad \text{Crosslinked polymer (5)}$$

(3) Disproportionation

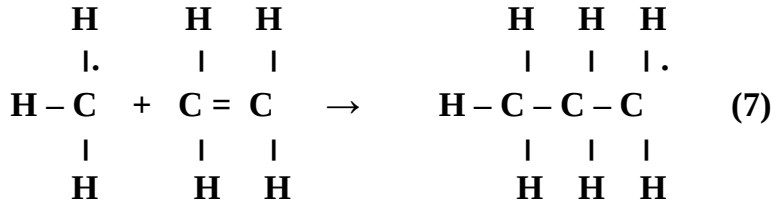
In this reaction, two radicals form a molecule transfer of an atom or group of atoms.

$$-CH_2-{}^{\bullet}CH- + -CH_2-{}^{\bullet}CH- \rightarrow -CH=CH- + -CH_2-CH_2- \qquad (6)$$

(4) Polymerization

A polymerization reaction occurs if a free radical can combine with another molecule without losing its characteristics. For example, a

methyl radical can combine with an ethylene molecule to form a propyl radical.



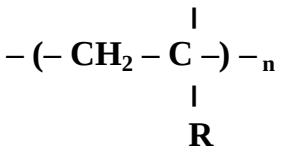
(7)

This radical can combine further with other ethylene molecules to form larger molecules. This process can continue until the radical reactivity is lost by recombination or disproportionation reactions with another radical. In general, the effect of radiation will depend only on the total quantity of energy deposited in the material, regardless of the nature of the incident photons or particles. The new chemical bonds formed are capable to alter the structure of the polymeric material and will result in changing the chemical and physical properties of the irradiated substances.

1.1.3. Radiation Crosslinking and Degradation of Polymers

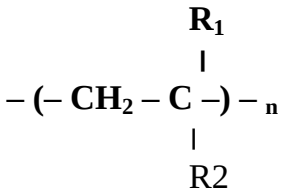
Chemical changes are important to understand the effect of radiation on polymers, which are the basis for the explanation of physical changes. The effect of radiation on polymer may bring about different types of reactions ***(Charlesby, 1953 and Sawallow, 1973).*** These reactions lead to the formation of chemical bonds between the polymer chain (crosslinking) and scission (degradation) of chemical bonds in polymer molecules. Radiolysis of high polymers have some other reactions such as gas evolution (hydrogen is always present), double bond formation and oxidation (in presence of oxygen, water and other oxygenated compounds). It has been observed that vinyl structure belong to the crosslinking type have the following structure:

H



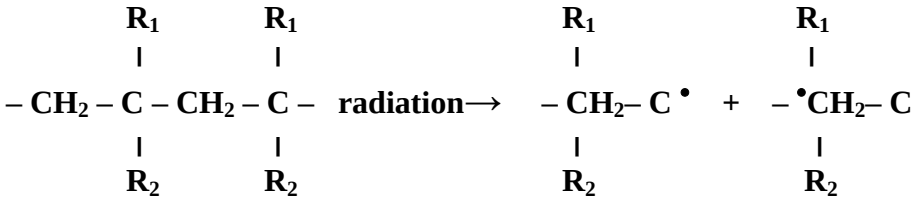
Structure (I)
(R may be hydrogen or other group)

On the other hand, polymers which undergo chain scission upon irradiation have structure (II).



Structure (II)
(R1 and R2 are not hydrogen)

When the structure of vinyl polymer is such that each carbon atom of the main chain carries at least one hydrogen atom, the polymer is crosslinking. However, if a tetra-substituted carbon atom is present in main chain the polymer degrades. The net result of crosslinking is increasing molecular weight of the polymer with increasing irradiation dose until a three dimensional network is formed, in which each polymer chain is linked with other at the middle of its length, as in reaction (5). Crosslinking may occur also due to recombination of free radicals formed by scission of C-C bonds, reaction with the participation of double bond and cyclization reaction. The general reaction for scission may be represented as follows;



The irradiation of polymers, like the irradiation of many other organic compounds, is accompanied in many cases by intense gas evolution. It was observed that the main gaseous product of the

radiolysis of crosslinking polymeric hydrocarbons is hydrogen. In degradation type polymers a large proportion of gaseous products are produced because of cleavage of the side groups at the quaternary carbon atom ***(Vereshchinskii and Pikaev, 1963).*** It was also reported that the yield of gas evolution is much higher if the radiation is carried out at high temperatures and particularly if the polymer is irradiated above its glass transition temperature.

Generally, the properties of polymers differ widely depending on whether the polymer crosslinks or degrades ***(Mariam et al, 2003).*** The irradiation of crosslinking type polymers increases the molecular weight until a completely network structure is formed accompanied with a gel formation. This was followed by an increase in elastic modulus and tensile strength and decrease in elongation. Polymers, which undergo degradation, show a decrease in molecular weight and viscosity.

1.2. Hydrogels

Hydrogels are a colloidal system in which a porous network of interconnected nanoparticles spans the volume of a liquid medium. In general, gels are apparently solid, jelly-like materials. Both by weight and volume, gels are mostly liquid in composition and thus exhibit densities similar to liquids; however has the structure of a solid. Gels can be loosely grouped along the following classes:

1 - Either inorganic or organic in nature.

2 - Having water (hydrogels), or an organic solvent (organogels).

3 - Being either colloidal or coarse in nature.

4 - As rigid gels, elastic jelly.

Hydrogels are the main class of gels. They have been since the discovery of poly (2-hydroxyethyl methacrylate) by Wichterle and Lim in 1960- ***(Peppas et al, 1986 and Luke et al, 2006)*** of great interest to biomedical scientists. They are defined as two or multi component systems consisting of three dimensional networked hydrophilic polymer chains which are capable of swelling in aqua's mediums and retaining a large amount of water or biological fluids ***(Peppas et al, 1987).*** Their ability to absorb water is due to the presence of hydrophilic groups such as (OH, CONH, $CONH_2$, COOH, and SO_3H along the polymer chain) ***(*Hinnerk, *2003).***

Hydrogels can exhibit both liquid like properties and solid like properties. Liquid like properties appear from the fact that the main constituent of it is water (some types of super absorbent hydrogels contain water up to 95% of its volume), while the solid like property is due to the network structure (the network structure is because of the presence of chemical or physical cross-linking of polymer chains)

1.2.1. Classification of Hydrogels

Hydrogels can be classified in several ways for example they can classified either as synthetic or natural according to their origin, degradable or stable depending on their stability characteristics, intelligent or conventional depending on their ability to exhibit significant dimensional changes with variations in pH, temperature, or electric field ***(Peppas, 1986).***

1.2.1.1. According to Method of Preparation *(Safaa et al, 2007)*

According to the method of preparation they are classified into four groups:

Homopolymeric Hydrogels

Homopolymeric hydrogels are composed of single type of monomers. The most known type of that gel is Poly (2-hydroxyethyl methacrylate), poly HEMA, which is used as soft contact lenses ***(Saraydin et al, 1995 and Azzam et al, 1980).***

Copolymeric hydrogels

Copolymeric hydrogels are an important class of biomaterials which consists of two types of components at least one is hydrophilic ***(Saraydin et al, 1995 and Azzam et al, 1980).***

Multi polymer hydrogels

This type of hydrogels consists of more than two types of components ***(Saraydin et al, 1995 and Azzam et al, 1980).***

Interpenetrating Polymer Network Hydrogels (IPNs)

The IPNs hydrogels are networks that contain two polymer systems, each in cross-link network. They can be defined as a combination of two or more polymer networks synthesized in juxtaposition ***(Sperling et al, 1998 and Xuequan et al, 2000).*** The presence of entangled crosslinks increases the miscibility of the polymers compared with that of usual blends and leads to material with good dimensional stability. The semi-IPNs differ from IPNs in that they are composed of a non-crosslinked polymer entrapped into another polymer network ***(Hee et al, 2001).*** IPNs now have gained more and more applications in industry and other fields, with IPNs showing the possibility for an even wider range of applications ***(Park et al, 1993).*** Studies of hydrogels are paid much attention, not only from chemical perspective, but also for their uses in chemical engineering, pharmaceuticals, food processing, biochemistry,

biology, and medicine. At present, most of researches about IPN hydrogels concern the intelligent hydrogel that can reversibly change their volume and shape in response to external stimuli, such as changes in pH and electric field. In terms of the super absorbent hydrogel, however, much interest has been focused on copolymeric or grafting copolymeric anionic hydrogels ***(Sperling et al, 1981 and Xuequan et al, 2000).***

1.2.1.2. According to Charge *(Ostroha et al, 2004)*

Non-Ionic hydrogels

Non-ionic hydrogels also known as neutral hydrogels, they are usually prepared of non charged networks.

Anionic hydrogels

This is to express the hydrogel witch contains negatively charged moieties. In the case of anionic polymeric network containing carboxylic or sulphonic acid groups, ionization takes place. The change in the pH of the external environment will act as a stimulus, and the response to the stimulus is the change in swelling properties of the hydrogels, causing the release of the protein lace, as the pH of the external swelling medium rises above the pKa of that ionizable moiety. That type of gels is usually swell at high pH, so anionic hydrogels are used in the design of intelligent controlled release devices for site-specific drug delivery of therapeutic proteins to the large intestine, where the biological activity of the proteins is prolonged ***(Am Ende et al, 1995).*** The change in the pH of the external environment will act as a stimulus, and the response to the

stimulus is the change in the swelling properties of the hydrogels, causing the release of the protein.

Hydrogels of poly(acry1ic acid) (PAA), and poly(acry1ic acid-co-2-hydroxyethyl methacrylate) [Poly(AA-co-HEMA)] hydrogels, were synthesized by **Ende and Peppas** ***(Am Ende et al, 1995)*** with varying degree of hydrophilicity and crosslinking density, and were studied as potential bio-adhesive controlled-release dosage forms. Equilibrium and dynamic swelling studies were carried out to determine the polymer mesh size and molecular weight between crosslinks of the hydrogels, in the ionized and non-ionized states. The PAA hydrogel mesh sizes ranged from 100 to 400 Å, over pH values of 3-7, whereas the Poly (AA-co-HEMA) hydrogel mesh sizes were between 13 and 140 Å. These results demonstrated the significance of the swelling medium pH on the hydrated state of the polymers, related to crosslinking or copolymerization composition.

Kim et al. ***(Am Ende et al, 1995)*** prepared pH sensitive anionic hydrogels based on poly (methacrylic acid-co-methacryloxyethyl glucoside) and poly (methacrylic acid-g-ethylene glycol). The hydrogels showed limited swelling in pH 2.2 buffers, but rapid swelling was observed in the pH 7.0 buffer solutions. The mechanism of water transport through the hydrogel was non-fickian at pH 2.2, and became relaxation controlled (case II) at pH 7.0 (higher than pKa of hydrogel)

Brazel and Peppas ***(Am Ende et al, 1995)*** studied hydrogels based on poly (N-isopropyl acrylamide- co-methacrylic acid). Heparin and streptokinase were loaded to study the release pattern, under pulsatile conditions of varying temperature and pH. The

hydrogels showed higher streptokinase release at pH 6.0 and 33°, and collapsed at pH 5.0 and 36°. But the same results were not observed in the case of heparin, which has smaller molecular diameter than streptokinase. It was concluded that the mesh size was too large to control the diffusion of heparin, even in the collapsed state.

The pH sensitivity of anionic hydrogels has been used to deliver proteins to the colon, where the activity of the proteolytic enzymes is comparatively lower. Calcitonin was loaded into hydrogels of poly (methacrylic acid-gethylene gethylene glycol) ***(Am Ende et al, 1995),*** and the release mechanism was found to be relaxation controlled, and calcitonin was released in 7 h. The hydrogels were prepared with different solvent volume fractions, ranging from 0.17 to 0.57. The calcitonin loading and the diffusion coefficient through the hydrogels decreased with increase in solvent volume fraction.

Kim and Peppas, studied Hydrogels of poly (methacrylic acid-comethacryloxyethyl glucoside) and poly (methacrylic acid-gethylene glycol) as a delivery system of insulin ***(Kim et al, 2000)***. The hydrogels showed slow release of insulin in acidic medium, and in alkaline pH, the release was rapid. The hydrogels were able to provide protective effect of insulin when treated with simulated gastric fluid.

Cationic hydrogels

Cationic hydrogels refers to the hydrogel witch contain positively charged moieties. The cationic hydrogels show swelling at pH values below pKa of the cationic group, at pHs greater than

pKa, the polymer is hydrophobic, and exclude water. Cationic hydrogels are used in the preparation of self regulated insulin delivery systems. The use of cationic hydrogels in the preparation of self-regulated insulin delivery systems has been reviewed by **Shivakumar and Satish *(Satish et al, 2003).***

Ampholytic Hydrogels

Polymeric ampholytic hydrogels are materials containing both cationic and anionic functional groups. They have received much recent attention because of their unique behavior ***(Flory, 1953, Young, 1991 and Allcock et al, 1990).*** The properties of polymeric ampholyte materials include a high degree of hydrophilicity, good biocompatibility, moderately high mechanical strength in the water-swollen state, and adjustable permeability to liquids depending on the type of fixed-charge groups present and the conditions of preparation.

There are two methods to prepare the ampholytic hydrogels:

(1) Copolymerizing an anionic monomer with a cationic monomer ***(Flory, 1949)***

(2) Incorporating a zwitterionic monomer into the hydrogel network **(Peppas et al, 1977).**

1.2.2. Synthesis of Hydrogels

Several techniques have been reported for the synthesis of hydrogels. The first approach involves copolymerization/crosslinking of monomers using multi-functional monomer, which acts as crosslinking agent. The polymerization reaction is initiated by chemical initiator. The polymerization

reaction can be carried out in bulk, in solution, or in suspension. The second method involves crosslinking of linear polymers by irradiation, or by chemical compounds ***(Rosiak, 1995 and Nodhov et al, 1994).***

Free-radical polymerization cross-linking is the preferred route used to prepare hydrogels especially from the class of acrylates, amides, and vinyl lactams ***(Tobita, 1993).*** It can also be used to prepare hydrogels from the naturally occurring polymers if the polymer backbone or chain end of the natural polymer has been functionalized with a radically polymerizable group. It is also the preferred route to prepare interpenetrating network hydrogels (IPNs) using either synthetic monomers or natural polymers (again functionalized with a radically polymerizable group). To form a hydrogel by free-radical polymerization, a difunctional crosslinking agent must be added to the polymerization. The chemistry of typical free-radical polymerizations involves an initiation, propagation, chain transfer and termination steps leading to the formation of a cross-linked polymer system. The initiation step (radical formation step) utilizes chemistries that when subjected to thermal or ultraviolet radiation form radicals that react with activated monomers such as a methacrylate. A wide variety of thermal, ultraviolet, visible and redox initiators are commercially available. Typical thermal initiators include the class of azo compounds such as azobisisobutylonitrile (AIBN) and peroxide initiators such as the peroxydicarbonates and the hindered peroctoates. The preparation of hydrogels by radiation treatment of aqueous solution of hydrophilic monomers or polymers carries some advantages over the

conventional techniques that it doesn't require initiators, crosslinkers and can be used practically with any vinyl monomer and both polymerization and crosslinking reactions can be initiated at ambient or sub-ambient temperatures.

Hydrogels can be prepared starting from monomers, prepolymers or existing hydrophilic polymers.

Synthesis of Hydrogels from Monomers (figure A).

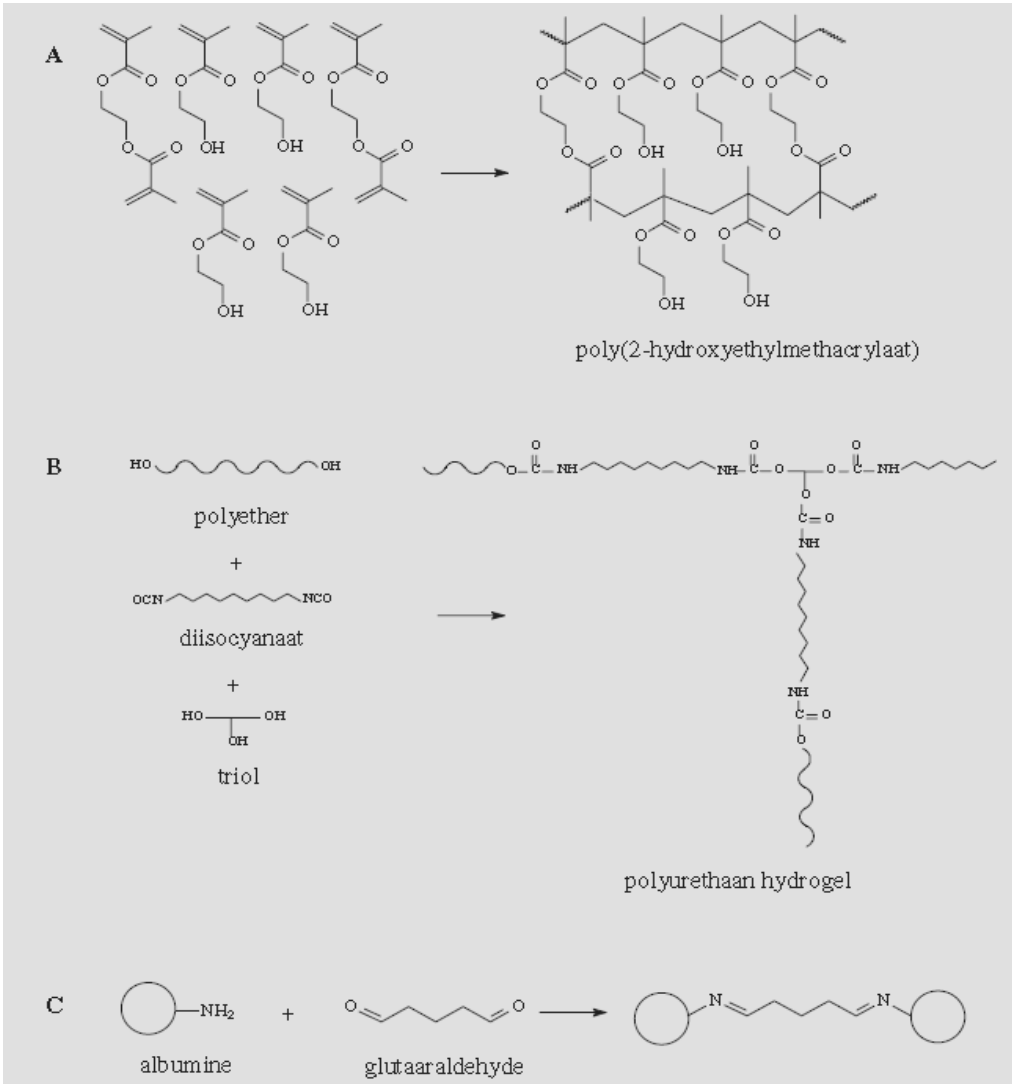
Copolymerization of hydrophilic monomers and poly-functional comonomers, acting as crosslinkers, leads to the formation of hydrophilic network structures.

Synthesis of hydrogels from Pre-polymers (figure B).

Hydrogels have been prepared by crosslinking of low molecular weight hydrophilic polymers or oligomers. One example is the reaction of α, ω-hydroxyl poly (ethylene glycol) with a diisocyanate in the presence of a triol as crosslinker [5,6]. This reaction leads to the formation of crosslinked hydrophilic polyurethanes.

Synthesis of hydrogels from Polymers (figure C).

Chemical crosslinking of hydrophilic polymers results in the formation of a hydrogel. There are numerous examples described in the literature. Well known is the preparation of stationary phases for gel filtration chromatography ***(Hagino et al, 1995)***



Preparation methods of hydrogels: starting from monomers (A), prepolymers (B) or existing hydrophilic polymers (C).

1.2.2.1. Physical Crosslinking

Physical hydrogels are three-dimensional structures held together by physical (non-covalent) junctions, In physical gels (pseudogels), the chains are connected by electrostatic forces, hydrogen bonds, hydrophobic interactions or chain entanglements, In contrast to covalent bonds, physical crosslinks usually do not act at a point on the chain but involve more extended junction zones, such gels are

non-permanent and usually they can be converted to polymer solutions by heating ***(Park et al, 1993).***

1.2.2.2. Polyelectrolyte Complexation

Generally, a polymer complex can be classified as a hydrogen-bonding complex, a polyelectrolyte complex (PECs), a stereocomplex, or a charged-transfer complex ***(Hegazy et al,2003).*** Polyelectrolyte complexes (PECs) are formed by the reaction of a polyelectrolyte with an oppositely charged polyelectrolyte in an aqueous solution. Complex hydrogels are prone to absorb large amounts of water and become swollen. The driving force is the water chemical potential difference between the polymer network and the aqueous phase ***(Peppas et al, 1976).***

The formation and properties of polymer complexes depend on the charge ratio of the anionic-to-cationic polymers, the degree of neutralization, the ionic strength, and the valences of the simple ions in the electrolyte solution ***(Hegazy et al, 2003).*** Therefore, a strong polyelectrolyte complex is obtained if the anions and cations in the polymers contain strong acids and bases, or if polyions attain their fully ionized forms. Conversely, a weak polyelectrolyte complex is formed in both weak acids and bases ***(Rosiak, 1995 and Nodhov et* al*, 1994).*** As an important class of polymer materials, they are widely used in many applications, such as membranes, medical prosthetics, antistatic coatings, environmental signals to the sensors, drug delivery systems, and for protein separation, etc. ***(Ng et al, 2003).*** A PEC with a high tendency of aggregation usually results when both the polyions have strong ionic groups and a good match

of charges. The PECs prepared from natural polymers, such as polysaccharides, have the additional advantage of being nontoxic and bio absorbable. ***(Lee et al, 2002).***

1.2.2.3. Hydrogen Bonding

The hydrogen bonds are only formed when the carboxylic acid groups are protonated. This implies that the swelling of these gels is strongly dependent on the pH. Poly (acrylic acid) and poly (methacrylic acid) form complexes with poly (ethylene glycol). These complexes are held together by hydrogen bonds between the oxygen of the poly (ethylene glycol) and the carboxylic group of poly (methacrylic acid), where as for poly (methacrylic acid) hydrophobic interactions also play a role ***(Israelachvili, 1985).*** Hydrogen bonding does not only occur between poly (methacrylic acid) and poly (ethylene glycol), but has also been observed in poly (methacrylic acid-g-ethylene glycol) ***(Salamone et al, 1985).*** Moreover, the complex of poly (methacrylic acid) and poly (ethylene glycol) prepared at low pH can be dissolved in ethanol. Upon injection, the diffusion of ethanol from the liquid transforms the system into a gel. The gel gradually dissolves in time due to dissociation of the complex ***(Guner, 1998 and Lugao et al, 2002).***

1.2.2.4. Chemical Crosslinking

Polymers containing functional groups like –OH, –COOH, –NH2, are soluble in water. The presence of these functional groups on the polymer chain can be used to prepare hydrogels by forming covalent linkages between the polymer chains and complementary reactivity,

such as amine-carboxylic acid, isocyanate-OH/NH2 or by Schiff base formation ***(Ratner et al, 1976).***

Gluteraldehyde can be used as a crosslinking agent to prepare hydrogels of polymers containing –OH groups like poly (vinyl alcohol) IB ***(Sperling et al, 1998*)**. Also, polymers containing amine groups (albumin, gelatin, polysaccharides) ***(Xuequan et al, 2000)*** can be crosslinked using gluteraldehyde. Polymers that are water soluble can be converted to hydrogels, using bis or higher functional crosslinking agents like divinylsulfone ***(Congming et al, 2003)*** and 1, 6-hexanedibromide ***(Herman et al, 2004).*** The crosslinking agents react with the functional groups present on the polymer, via addition reaction. These crosslinking agents are highly toxic, and hence un-reacted agents have to be extracted. Moreover the reaction has to be carried out in organic solvent, as water can react with the crosslinking agent. The drugs have to be loaded after the hydrogels are formed, as a result the release will be typically first order.

Crosslinking between polymers through hydrogen bond formation occur as in the case of poly(methacrylic acid) and poly(ethylene glycol). The hydrogen bond formation takes place between the oxygen of poly(ethylene glycol) and carboxylic acid group of poly(methacrylic acid) ***(Israelachvili, 1985).*** Carriers consisting of networks of poly(methacrylic acid-gethylene glycol) showed pH dependent swelling due to the reversible formation of interpolymer complex, stabilized by hydrogen bonding between the etheric groups of the grafted poly(ethylene glycol), and the carboxylic acid protons of the poly(methacrylic acid) ***(Marey et al, 1995).***

1.2.2.5. Ionizing Radiation

High energy radiation like gamma and electron beam, have been used to prepare the hydrogels of unsaturated compounds. The irradiation of aqueous polymer solution results in the formation of radicals on the polymer chains. Also, radiolysis of water molecules results in the formation hydroxyl radicals, which also attack the polymer chains, resulting in the formation of macroradicals. Recombination of the macroradicals on different chains results in the formation of covalent bonds, and finally a crosslinked structure is formed ***(Menemse et al, 2005).*** During radiation, polymerization macroradicals can interact with oxygen, and as a result, radiation is performed in an inert atmosphere using nitrogen or argon gas. Examples of polymers crosslinked by radiation method include poly(vinyl alcohol) ***(Sen et al, 1999),*** poly (ethylene glycol) ***(Erdener et al, 2006)***, poly(acrylic acid). Among various methods applied for the production of hydrogels, the radiation technique has many advantages, as a simple, efficient, clean and environment-friendly process. It usually allows combining the synthesis and sterilization in a single technological step, thus reducing costs and production time ***(Sen et al, 2005).***

(Razzak et al, 1999) had obtained Sequential net-PP-g-PNIPAAm-inter-net-PAAc by γ-radiation and resulted in both temperature and pH-sensitivity, with LCST 33^{o}C and critical pH 6.2. The grafting of PP films with IPNs of PAAc and PNIPAAm enables one to tune the amount of vancomycin loaded as well as the drug release rate. Therefore, this approach may well be useful to modify

the surface of PP-based medical devices, in order to reduce the likelihood of infections associated with their clinical use**.**

(Bordi et al, 2002) synthesized polyampholytic and Reversible pH-Responsive hydrogels, CS-g-poly (AAc-co-AAm) by γ-radiation induced polymerization and crosslinking. The swelling of hydrogel exhibited high sensitivity to pH. Study effect of H+/OH- concentration carried out at various pH shows that the swelling of hydrogel causes several large volume changes. Ionic repulsion between charges groups incorporated in the gel matrix by an external pH modulation could be assumed as the main driving force responsible for such swelling changes. Investigating the ability of the prepared polyampholytic network to be used as a carrier for drug deliver system showed a promising result not only in the field of drug targeting but it also shows the possibility of controlling the released amount and release rate. Polyampholytic and pH-Responsive Hydrogel by radiation process with suitable amoxicillin release profiles for site-specific antibiotic delivery in the stomach.

(Yoshiro et al, 2006) prepared Thermo sensitive membranes by radiation-induced graft copolymerization of monomers on PET fabrics. A binary mixture of N-isopropyl acrylamide (NIPAAm) and acrylic acid (AAc) was grafted on polyester fabric as a base material to introduce thermo sensitive poly (N-isopropyl acrylamide) pendant chains having LCST slightly higher than 37^{o}C in the membrane. The influence of ferrous sulfate, radiation dose and monomer composition on the degree of grafting was studied. The structure of the grafted fabric was characterized by thermo gravimetric analysis, differential scanning calorimetry and scanning electron microscopy.

The thermo sensitive nature of the fabric was monitored by swelling at different temperatures. The graft copolymerization of AAC with NIPAAm enhanced the LCST of the resultant membrane to 37^{o}C. The moisture vapor transmission rate (MVTR) and air permeability of the fabric decreased slightly may be due to the slight blocking of the fabric pores. The immobilization of tetracycline hydrochloride as the model drug and its release characteristics at different temperatures were monitored.

Studies have been made by ***(Hegazy et al, 2004)*** for the preparation and characterization of different hydrogels and membranes which are prepared by γ-radiation-induced copolymerization and grafting of different vinyl and acrylic monomers such as acrylic acid (AAc), 4-vinylpyridene (4-VP), AAc/ 4-VP, N-vinyl pyrrolidone/acrylic acid (NVP/AAc) and NVP/Acrylamide (NVP/AAm) for the purpose of separation and extraction of some heavy and toxic metal ions as well as dyes from wastewater ***(Declan et al, 2005)***. The factors affecting the preparation and homogeneity of such prepared materials were thoroughly investigated. Characterization, stimuli-responsive and some selected properties of the prepared hydrogels and membranes were studied and accordingly the possibility of its practicable uses in separation processes and wastewater treatment were thoroughly studied and determined.Also, several trials were made to improve the chelation affinity and adsorption capacity to the metals by further introduction of certain reactive chelating groups via the functional groups of the prepared hydrogels and membranes. It is worthy to mention that different natural lingo- cellulosic materials

were also used for the preparation of super-adsorbent materials suitable for separation and purification processes of wastewater. Also, trials were made for the recovery of valuable metals for their waste such as Au, Ag and Ru. Some of the radiation prepared hydrogels and membranes showed very promising stimuli-responsive properties which make them of practicable uses.

(Pengfei et al, 2002) carried out the preparation of PEO hydrogels by g-ray irradiation, and then grafting by AAc monomer onto the PEO hydrogels with subsequent irradiation. The degree of grafting of these hydrogels increased as the concentration of AAc monomer increased. The equilibrium swelling measurements of these hydrogels, which were carried out in SGF and SIF, showed a pH-sensitive nature. The oral administration of insulin-loaded hydrogels to rats decreased the blood glucose levels for at least 4 h due to the absorption of insulin in the GI tract. Hydrogels could be applied for the successful oral insulin delivery to the GI tract.

(Abdel-Azim et al, 2004) prepared PVA /PVP blended hydrogel by using γ-rays irradiation technique. PVA and PVP can form a thermodynamically miscible pair. FTIR and DSC confirmed the miscibility and compatibility of PVA/PVP hydrogel. The gel fraction increases with increasing irradiation dose, while the swelling of PVA/PVP hydrogel nearly tends to increase with increasing PVP content and reduced with enhanced irradiation doses. PVA/PVP with compositions 80/20 and 70/30 were selected to be used as materials that have antimicrobial activity. Irradiation dose of 30 kGy was found to have an advantage on other tried doses concerning.

The radiolytic formation of Ag nanoparticles in crosslinked PVA hydrogel was investigated by ***(Karayannidis et al, 2005).*** The reduction of Ag+ ions was performed using strongly reducing species such as hydrated electrons, propan-2-ol and PVA radicals. Ag+ ions were efficiently reduced in swollen PVA matrix by PVA radicals. Thermal and thermooxidative properties of radiolytically obtained nanocomposites were affected by the content of nanofiller as well as by different routes of preparation

Hydrogels, in general, can be used as a compliant surface in prosthesis of human synovial joints due to their biocompatible characteristics. In this work***, (Ronny et al, 2005)*** prepared different hydrogels from two aqueous solutions of PVA (15 and 20 mass/mass%) by chemical reactions using citric acid as a cross-linking agent and by electron beam (EB) irradiation with doses from 25 to 100 kGy. The main effort of the work was the development of a new material to be used as artificial articular cartilage. From the obtained experimental results, it can be concluded that the PVA hydrogels produced by irradiation cross-linking process have lower water absorption capacity, better mechanical properties and higher thermal stability when compared with hydrogels obtained through a chemical cross-linking process with citric acid.Furthermore, it was found that radiation doses above 25 kGy did not produce drastic changes on the mechanical and thermal properties of the irradiated PVA hydrogels. It is worth mentioning that the radiation process cross-links and sterilizes the hydrogels simultaneously The hydrogels were evaluated by their mechanical properties through

indentation creep test, thermal properties by differential scanning calorimetry (DSC), and also equilibrium water content (EWC).

(Young et al, 1991) have developed a novel method for the preparation of size controlled and monodisperse PEG nanoparticles using liposomes as templates. Large liposomes block the entrance to the pores of the membrane and break up easily at the pore because of the flexibility and relative weakness of the lipid bilayer of liposomes. Therefore, monodisperse liposomes whose size is comparable to the pore size can be produced and the PEG hydrogel solution inside the liposome can be polymerized by UV irradiation. The prepared PEG nanoparticles were highly monodispersed compared with PEG nanoparticles without extrusion. The PEG nanoparticles could be functionalized to react with amine-bearing materials by grafting PEG derivatives with aldehyde functional groups, and β-gal enzymes were immobilized in the PEG particles without losing their activity. The procedures for preparation of nanoparticles and surface modification/enzyme immobilization could be performed simultaneously. This technique is also appropriate for the mass production of homogeneous polymer nanoparticles. We believe that the preparation of polymer nanoparticles using this technique will be useful for producing monodisperse polymer nanoparticles with specific sizes for applications such as specific drug delivery/ targeting, coating for biosensors, contrast agents for imaging, and scaffolds for tissue engineering.

1.2.3. Applications of Hydrogels

1.2.3.1. Responsive Hydrogels

Environmentally responsive hydrogels have been synthesized that are capable of sensing and responding to changes to external stimuli, such as changes to pH 1, and temperature ***(Am Ende et al, 1995).*** The response mechanism is based on the chemical structure of the polymer network (e.g., the functionality of chain side groups, branches, and crosslinks). For example, in networks that contain weakly acidic or basic pendent groups, water sorption can result in ionization of these pendent groups depending on the solution pH and ionic composition

For ionic gels containing weakly acidic pendent groups, the equilibrium degree of swelling increases as the pH of the external solution increases, while the degree of swelling increases as the pH decreases for gels containing weakly basic pendent groups. Temperature-responsive hydrogels are one of the most widely studied responsive hydrogel systems. These systems, which are mostly based on poly (N-isopropylacrylamide) (PNIPAAm) and its derivatives, undergo a reversible volumephase transition with a change in the temperature of the environmental conditions. This type of behavior is related to polymer phase separation as the temperature is raised to a critical value known as the lower critical solution temperature (LCST). Networks showing a lower critical miscibility temperature tend to shrink or collapse as the temperature is increased above the LCST, and the gels swell upon lowering the temperature below the LCST.

1.2.3.2. Drug Delivery Hydrogels

A series of poly [(N-isopropylacrylamide)-co-(methacrylic acid)] (P [(N-iPAAm)-co-(MAA)]) hydrogels was investigated to determine the composition that exhibits a better pH modulated release of diltiazem hydrochloride (DIL.HCl). For this purpose hydrogel slabs were loaded with DIL.HCl by the immersion method, and its release under acidic medium (0.1N HCl, pH 1.2) and in phosphate buffer pH 7.2, using United States Pharmacopeia (USP) 24 Apparatus 1, was investigated. The release of DIL.HCl from P [(N-iPAAm)-co-(MAA)] hydrogels depends strongly on the copolymer composition. Enriched N-iPAAm hydrogel slabs would prevent DIL.HCl release in the stomach allowing drug release at the higher pH of the gastrointestinal tract. These facts indicate that enriched N-iPAAm hydrogels are suitable to be used as pH-modulated drug delivery systems. Controlling particle size in 85% mol N-iPAAm hydrogel tablets allows tailoring of the release rate of DIL.HCl. A relationship exists between release rate and particle diameter[Eva Díez-Peña,1 Paloma Frutos,2 Gloria Frutos,3 Isabel Quijada-Garrido,1 and José Manuel Barrales-Rienda1The Influence of the Copolymer Composition on the Diltiazem Hydrochloride Release From a Series of pH-sensitive Poly[(N-isopropylacrylamide)-co-(methacrylic acid)] ***(Peppas et al, 1977).***

Novel microstructure and pH sensitive poly (acryliac acid-co-2-hydroxyethyl methacrylate) / poly (vinyl alcohol) (P (AA-co-HEMA)/PVA) interpenetrating network (IPN) hydrogel films were prepared by radical precipitation copolymerization and sequential IPN technology. The first P (AA-co-HEMA) network was

synthesized in the present of PVA aqueous solution by radical initiating, then followed by condensation reaction (Glutaraldehyde as crosslinking agent) within the resultant latex, it formed multiple IPN microstructure hydrogel film. The film samples were characterized by IR, SEM and DSC. Swelling and deswelling behaviors and mechanical property showed the novel multiple IPN nanostructure film had rapid response and good mechanical property. The IPN films were studied as controlled drug delivery material in different pH buffer solution using cationic compound, crystal violet as a model drug. The drug release followed different release mechanism at pH 4.0 and pH 7.4, respectively ***(Yazdani et al, 2004).***

1.2.3.3. Biomaterial Hydrogels

PEG hydrogels are one of the most widely studied and used materials for biomedical applications. PEG hydrogels are nontoxic, non-immunogenic, and approved by the US Food and Drug Administration for various clinical uses. In many cases, PEG has been applied as a "stealth material" since it is inert to most biological molecules such as proteins. Some of the earliest work on the use of PEG and poly (ethylene oxide) (PEO) as hydrophilic biomaterials was performed by ***(Michal et al, 1999)*** who showed PEO adsorption onto glass surfaces prevented protein adsorption. Since then, many forms of PEG surface modification have been used in order to render a surface protein resistant and to enhance surface biocompatibility ***(Begam et al, 2003).*** Commonly used methods of PEG surface modification include covalent bonding through silane,

acrylate, and thiol linkages, adsorption, and ionic and hydrogen bonding, all of which have been reviewed elsewhere ***(Begam et al, 2003)*** PEG polymers can be covalently crosslinked using a variety of methods to form hydrogels. A particularly appealing method of crosslinking PEG chains is through photopolymerization using acrylate-terminated PEG monomers ***(Saha et al; 2000 and Virk, 2002).*** In the presence of cells, PEG hydrogels are passive constituents of the cell environment since they prevent adsorption of proteins. However, numerous methods of modifying PEG gels have made PEG gels a versatile template for many subsequent conjugations. For example, peptide sequences have been incorporated into PEG gels to induce degradation ***(Singh and Singh, 2004).*** In addition to chemical modification, block copolymers of PEG, such as triblock copolymers of PEO and poly(propylene oxide) (henceforth designated as PEO-b-PPO-b-PEO), degradable PEO, poly(lactic acid) (PLA), and other similar materials, can be used to add specific properties to the PEG hydrogels ***(Cataldo, et al 2004)***.

Another major synthetic polymer is PVA ***(Mariam et al; 2003).*** PVA hydrogels are stable, and elastic gels that can be formed by the repeated freezing and thawing process or chemically crosslinked ***(Peppas, 1986 and Luke et al, 2006)*** They can be formed by both physical and chemical crosslinking methods ***(Peppas et al, 1997).*** The physically crosslinked versions of PVA hydrogels are biodegradable, and thus can be used for various biomedical applications ***(Peppas, 1997 and Sperling, 1998 and Xuequan et al, 2000).*** PVA must be crosslinked in order to be useful for a wide

variety of applications, specifically in the areas of medicine and pharmaceutical sciences. Crosslinking may be achieved by chemical, irradiative, or physical mechanisms. PVA can be crosslinked through the use of difunctional crosslinking agents. Some of the common crosslinking agents that have been used for PVA hydrogel preparation include glutaraldehyde, acetaldehyde, formaldehyde, and other monoaldehydes. When these crosslinking agents are used in the presence of sulfuric acid, acetic acid, or methanol, acetal bridges form between the pendent hydroxyl groups of the PVA chains. As with any crosslinking agent, however, residual amounts are present in the ensuing PVA gel. It becomes extremely undesirable to perform the time-consuming extraction procedures in order to remove this residue. If the residue is not removed, the gel is unacceptable for biomedical or pharmaceutical applications because, if it were placed directly in the body, the release of this toxic residue would have obvious undesirable effects. Other methods of chemical crosslinking include the use of electron-beam or gamma irradiation. These methods have advantages over the use of chemical crosslinking agents as they do not leave behind toxic, elutable agents. In addition, photocrosslinkable PVA hydrogels have been synthesized that facilitate cell adhesion in tissue-engineering applications ***(Hee, 2001 and Park, 1993)***. In this work, they have evaluated the potential for novel poly (vinyl alcohol)–poly(acrylic acid) freeze the composite hydrogels for use as a wound dressing with the capability of delivering aspirin to the wound. The research showed that the incorporation of APIs, in this case aspirin, can have a significant effect on the overall mechanical properties of freeze/thaw PVA/PAA hydrogels. The effect of incorporating aspirin within the hydrogel led to a decrease in the

mechanical properties of the overall structure. To compensate for this loss in mechanical strength, a novel hydrogel-film composite was produced. The film acted as a reinforcing film within the hydrogel. From DSC analysis carried out it was evident that aspirin had a plasticizing effect effectively lowering the Tg of the PVA within the gels by more than 25 ◦C. From solvent uptake studies carried out it was observed that less swelling occurred in media of pH 4 than in pH 9. This is due to the pH-sensitive nature of the hydrogel caused by the addition of PAA and aspirin which contain reactive groups. Anomalous or non-Fickian transport was the predominant release mechanism for these hydrogels. The novel composites produced in this study have particular potential in wound care, specifically scar limitation ***(Hoffman, 1987).***

1.2.3.4. Applications in Agriculture

1.2.3.5. Wastewater Treatments

Hydrogels based radiation crosslinking crosslinkable polymer (PAAc) and a radiation degradable polymer (sodium alginate) were successfully prepared by ***(Nizam El-Din et al, 2007)*** under the effect of gamma irradiation. The interpenetrating hydrogels were evaluated as responsive and metal sorbet materials. The TGA study revealed that the AAc/AG hydrogels possess a lower thermal stability than pure PAAc hydrogel. The results indicate that the hydrogels composition is an effective parameter in determining the metal sorption character. In this regard, the hydrogel based on PAAc displayed higher affinity for copper ions, while AAc/AG hydrogels showed higher affinity for cobalt and nickel ions.