



A review on the radiation synthesis of copolymeric hydrogels for adsorption and separation purposes¹

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Abstract

Recent theoretical and experimental work on the radiation synthesis, characterization and the use of hydrogels containing diprotic acid moieties have been reviewed. It is shown that upon incorporating vinyl monomers carrying diprotic acid groups randomly in the main chain, non-ionic hydrogels like poly(acryl amide) and poly(*n*-vinyl 2-pyrrolidone) acquired stimuli-responsive behaviours. The swelling behaviours of these hydrogels are shown to be predictable reliably under varying solution conditions by a theoretical expression derived recently. Examples are given for the utilization of these hydrogels in the adsorption and separation of biomolecules, dyes and metal ions in aqueous media and their ability to release drugs in stepwise manner in response to pH of the environment. © 1999 Elsevier Science Ltd. All rights reserved.

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1. Introduction

Hydrophilic polymers when cross-linked chemically or physically forming three dimensional networks swell but do not dissolve in water. They are termed hydrogels when the amount of water retained is between 20–100% of the total weight, and when water content exceeds 100% these hydrogels are called superadsorbent hydrogels. 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(hydroxy 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.

Recently hydrogels have found a wide range of biomedical applications including controlled drug delivery systems, replacement 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

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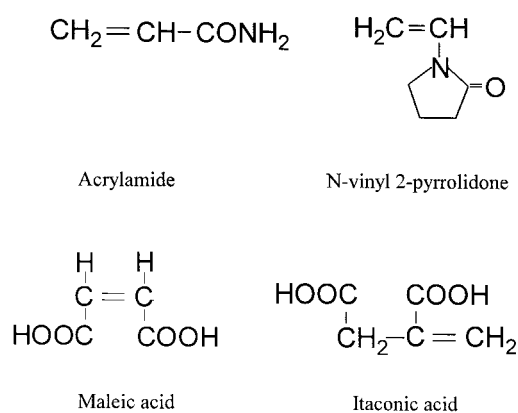
¹ Dedicated to Professor Joseph Silverman on the occasion of his 75th birthday.

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 are commonly used as burn and wound dressing materials (Rosiak et al., 1995). They prevent microbial contamination of the wound, inhibit the loss of body fluids and provide free flow of oxygen to the wound and generally accelerate the healing process.

The most characteristic property of hydrogels is their ability to swell in the presence of water and to shrink in the absence of it. The two most important factors controlling the extent of swelling are the hydrophilicity of polymer chains and the cross-link density. By incorporating some stimuli-responsive comonomers either into the backbone of the network structure or as pendant groups it is possible to prepare hydrogels with responsive properties. These hydrogels possess the ability to swell, shrink, bend or even degrade in response to a signal. These stimuli-responsive hydrogels are also called intelligent hydrogels. They reversibly swell and shrink with small changes in the environmental conditions. The most common environmental factors that causes an abrupt volume changes in hydrogels are pH, temperature, electric field, ionic strength and type of salt. In addition to wide range of applications of these hydrogels in biomedical applications, they are also used in the separation and purification processes.

Hydrogels are typically synthesized by one of the two well established procedures: (a) polymerization and simultaneous or postpolymerization cross-linking of hydrophilic monomers, and (b) modification of hydrophilization of existing polymers with potential hydrogel properties. A comprehensive review of the chemistry and various synthetic approaches used in hydrogel preparation can be found in the compilation of Peppas (1987). A more recent review by Mathur et al. (1996) provides an in depth discussion on the methods of hydrogel synthesis. The inherent advantages of using high energy radiation in the synthesis of hydrogels for biomedical applications have been reviewed by Carena (1992). The preparation of hydrogels by radiation treatment of aqueous solutions of hydrophilic monomers or polymers carries some advantages over the conventional techniques. It does not require initiators, cross-linkers and can be used practically with any vinyl monomer and both polymerization and cross-linking reactions can be initiated at ambient or sub-ambient temperatures.



Scheme 1.

Responsive behaviour of hydrogels make them also very attractive materials for some specific applications in adsorption, enrichment and separation processes. Sites showing selectivity for proteins, enzymes, biomolecules or dyes, pigments or metal ions can be easily incorporated into network structure by radiation induced polymerization. During the last decade a number of papers published from this laboratory showed clearly the advantages of irradiating aqueous monomer solutions to synthesize copolymeric hydrogels. In this context the use of even very small quantities of diprotic acid-containing monomers proved to impart fascinating properties to the hydrogels of starting monomers homopolymers. The present paper aims to make a comparative assessment on the utilization of copolymeric hydrogels prepared from acrylamide and N-vinyl 2-pyrrolidone as base monomers and itaconic acid and maleic acid as comonomers.

2. Experimental

Two hydrophilic monomers used as base monomers in the synthesis of hydrogels, acrylamide (AAm) and N-vinyl 2-pyrrolidone (VP) were obtained from BDH and Fluka respectively. The comonomers carrying diprotic acid groups, namely itaconic acid (IA) and maleic acid (MA) were products of BDH Chemicals Ltd. The chemical formula of these monomers are given in Scheme 1.

A range of compositions for pairs of base monomer and comonomer prepared in distilled water and these solutions were irradiated with γ -rays at a dose rate of 0.75 kGy/h from Co-60 γ -irradiator of Gammacell 220 type at ambient temperature to doses 2.00–5.70 kGy. Further details on the preparation and characterization of copolymeric hydrogels can be found in the work of Saraydin et al. (1995a). Cross-linked copolymers obtained in long cylindrical shapes in elastomeric form

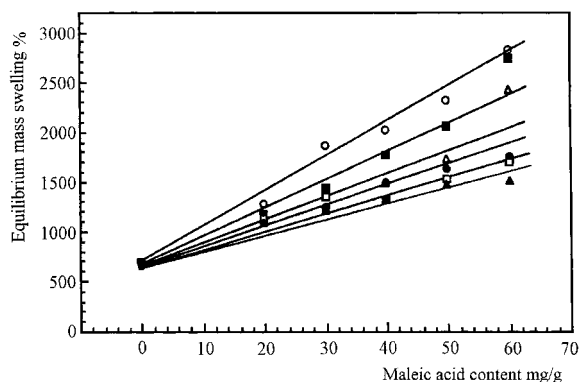


Fig. 1. Variation of equilibrium mass swelling % with MA content in hydrogels: (○) 2.00 kGy; (■) 2.60 kGy; (△) 3.73 kGy; (●) 4.65 kGy; (□) 5.20 kGy; (▲) 5.71 kGy (Saraydin et al., 1995a).

were cut into pieces of approx. 3 mm length. They are thoroughly washed with water, dried first with filter paper then in air and vacuum for further usage. Various dyes, metal ions and biomolecules were used in adsorption studies.

3. Results and discussion

Despite availability of enormous number and variety of synthetic vinyl monomers, there are just a few hydrophilic monomers from which hydrogels can be prepared. Among them 2-hydroxy ethyl methacrylate, acrylamide and N-vinyl 2-pyrrolidone comprise the three most frequently used. Poly(ethylene oxide) and poly(vinyl alcohol) are the two polymers preferred in the synthesis of hydrogels. In order to incorporate stimuli-responsive properties to the hydrogels prepared

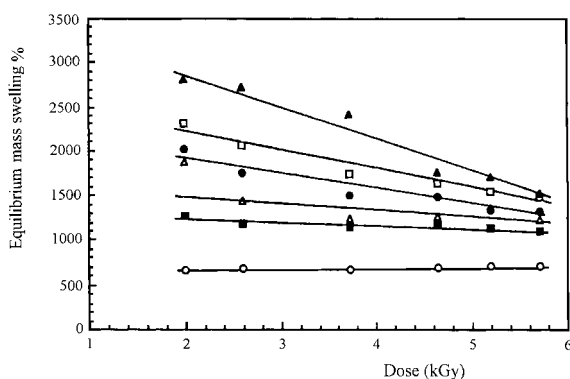


Fig. 2. Variation of equilibrium mass swelling % in hydrogels with the irradiation dose: (○) 0 mg MA; (■) 20 mg MA; (△) 30 mg MA; (●) 40 mg MA; (□) 50 mg MA; (▲) 60 mg MA (Saraydin et al., 1995a).

from above mentioned monomers or polymers radiation copolymerization and/or grafting with monomers carrying appropriate properties are generally considered. This constitutes the main approach followed in the preparation of copolymeric hydrogels in the present work.

For non-ionic hydrogels the swelling is controlled by the hydrophilicity of the base monomer or polymer and the density of the intermolecular cross-links. These effects are illustrated in Figs. 1 and 2 where the influence of comonomer and dose on the swelling capacity of diprotic acid-containing hydrogels are shown. With the introduction of mono or diprotic acidic groups into the main chain, pH of the solution becomes even more important factor determining the swelling kinetics and equilibrium swelling value. The analysis of swelling for non-ionic hydrogels is mostly based on the theories of Flory and Rehner (1943). Their equations have been widely used to characterize the polymeric networks prepared either from polymers or mixture of monomers. The Flory–Rehner model consider a situation where cross-links are randomly introduced in the dry stage. Peppas and Merrill (1976) derived a model which accounts for the introduction of cross-links in the relaxed state as in the case of solution polymerization. Both of these models deal with neutral polymer networks. When the chains forming the network contain ionizable groups, the forces influencing swelling are greatly increased due to localization of charges within the hydrogel. The equilibrium swelling ratios attained are often an order of magnitude larger than those of neutral networks, as intermolecular coulombic, hydrogen bonding and polar forces are significantly present. By including the influence of ionic contribution to forces arising from mixing and elastic-retraction of chains, Brannon-Peppas and Peppas (1991) have predicted the theoretical swelling behaviour of ionic hydrogels. In a recent article we have published equations to predict the swelling of hydrogel, with diprotic acid moieties as a function of polymer, solvent and solution based parameters. The derivation of predictive equation was based on the approach of Peppas with the introduction of phantom network model of Erman and Flory since in the highly swollen state a real network exhibits properties closer to those of the phantom network model. The equation describing the total free energy change for an ionic network placed in a swelling agent is given as:

$$\Delta G = \Delta G_{\text{mix}} + \Delta G_{\text{el}} + \Delta G_{\text{ion}} \quad (1)$$

which can be written in terms of chemical potentials by taking the derivative of each term with respect to the number of molecules of swelling agent in the system. For the ΔG_{mix} term, Flory–Huggins relationship; for ΔG_{el} , respective equation valid for a phantom net-

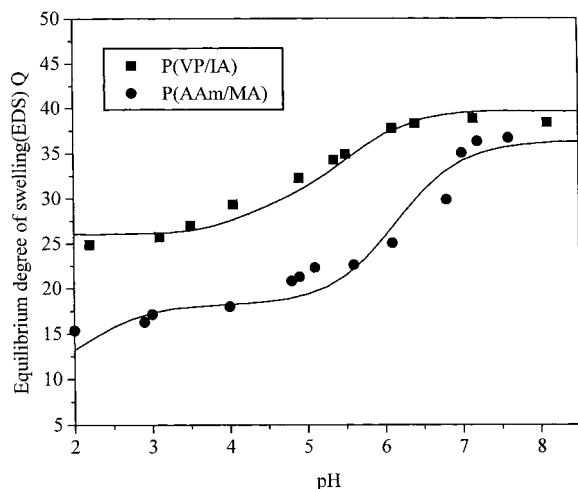


Fig. 3. Effect of pH on the equilibrium degree of swelling of *P(VP/IA)* and *P(AAm/MA)* copolymeric hydrogels (solid curves are theoretical predictions drawn according to Eq. (2) (Şen and Güven, 1998).

work are substituted. The ionic contribution is calculated by using the equation derived by Brannon-Peppas and Peppas (1991) by considering the primary (K_{a1}) and secondary onization (K_{a2}) of diprotic acids, the weight fraction of ionizable polymer in the network (X), the ionic strength of the medium (I) and the degree of ionization (i). Following is the final form of the equation used in the prediction of swelling behaviour of diprotic acid containing hydrogels (Şen and Güven, 1998):

$$\left(\frac{[2K_{a1}K_{a2} + 10^{-\text{pH}}K_{a1}]}{2[(10^{-\text{pH}})^2 + 10^{-\text{pH}}K_{a1} + K_{a1}K_{a2}]} \right)^2 \left(\frac{V_1 v_{2m}^2 X^2}{4\bar{v}^2} \right) = \ln(1 - v_{2m}) + v_{2m} + \chi v_{2m}^2 + \frac{(1 - 2/\phi)V_1 v_{2r}^{2/3} v_{2m}^{1/3}}{\bar{v}M_c} \quad (2)$$

where, V_1 is the molar volume of swelling agent, v_{2m} is the polymer volume fraction in the equilibrium-swollen system, \bar{v} is the specific volume of the polymer, v_{2r} is the polymer volume fraction in the relaxed state (that means after cross-linking but before swelling), χ is the Flory–Huggins polymer–solvent interaction parameter, ϕ is the functionality at the cross-linking site, M_c is the number average molecular weight between consecutive cross-links.

The above equation has enabled us to theoretically predict swelling behaviour of hydrogels containing diprotic acid moieties under a number of polymer-based parameters, solution property parameters and polymer–solvent combination type parameters. By re-

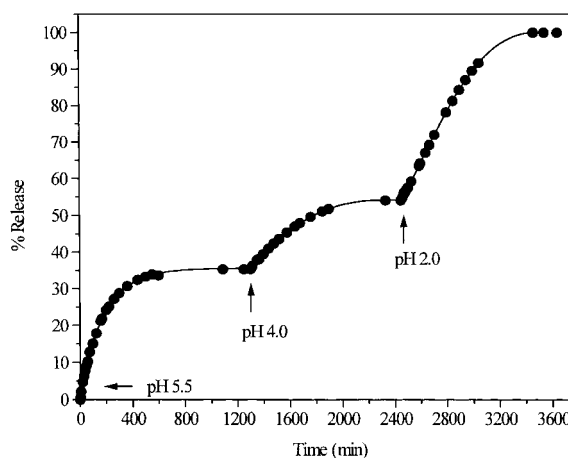


Fig. 4. Release of specific adsorbed Methylene Blue from *P(VP/IA)* hydrogels (Şen and Güven, 1999c).

arranging Eq. (2) it was also possible to determine simultaneously the average molecular weight between cross-links, and the polymer–solvent interaction parameter from the equilibrium swelling data. These theoretical approaches have been verified in our work to compare the experimental and theoretical swelling behaviours of acrylamide/maleic acid and N-vinyl 2-pyrrolidone/itaconic acid copolymeric hydrogels (Şen et al., 1999a). The response of these types of poly-electrolyte hydrogels can be satisfactorily predicted against some external stimuli (Şen and Güven, 1999b) as well. The incorporation of diprotic acid moieties into hydrogel network imparts a stepwise response in terms of swelling or deswelling of these gels undervarying pH conditions. The theoretical and experimental results for the swelling of maleic and itaconic acid containing hydrogels are given in Fig. 3. The strong influence of pH on the controlled release behaviours of poly(N-vinyl 2-pyrrolidone/itaconic acid) hydrogels has recently been shown on some model drugs (Şen and Güven, 1999c). The effect of pH on the release of a model drug Methylene Blue from poly(N-vinyl 2-pyrrolidone/itaconic acid) hydrogels are clearly seen from Fig. 4. Similar copolymeric hydrogels were shown to be very useful in the immobilization of enzymes such as α -amylase (Şen et al. 1999d).

Environment sensitivity or control of swelling ability of poly-electrolyte hydrogels under a variety of external conditions make them ideal adsorbents for removal, adsorption on enrichment of some water soluble agents such as proteins, biomolecules, metallic impurities, dyes, etc. Novel applications of hydrogels in bioseparation or as intelligent artificial systems have been widely presented in the recent literature (Ottonbrite et al., 1996). The hydrogels based on poly-electrolyte structures and synthesized via irradiation of

aqueous solutions of acrylamide and N-vinyl 2-pyrrolidone with small quantities of maleic or itaconic acids are regarded as systems with potential immobilization, chelating and adsorptive properties for various bioapplications. The capacity of those gels to adsorb Bovine Serum Albumin (BSA) was investigated by using gels with varying compositions of maleic acid (Saraydın et al., 1994) and itaconic acid moieties (Karadağ et al., 1994). An increase in the content of diprotic acids has led to increased adsorption of BSA. It has also been determined that by controlling external conditions, the BSA uptake of these hydrogels were enhanced (Akkaş et al., 1999). In order to evaluate biocompatibility of these gels, they were incubated in human serum and their biocompatibility with some biochemical parameters were controlled (Saraydın et al., 1995b; Karadağ et al., 1996a). Acrylamide/itaconic acid hydrogels have been determined to be efficient adsorbents for nicotine and nicotine derivatives (Karadağ et al., 1997).

Polymeric substrates are being continuously developed and used for the purpose of complexation with metal ions either for ion-exchange or selective adsorption purposes. These polymeric ligands are tailor synthesized to remove certain metal ions or groups from aqueous media. The introduction of maleic or itaconic acid type monomeric units into acrylamide and N-vinyl 2-pyrrolidone based hydrogels imparted chelating properties into these hydrogels. The complexation of these diprotic acidic groups with some heavy metal ions provided an efficient way of their removal from aqueous systems (Saraydın et al., 1995c). Same hydrogels were proven to be very effective in the uptake of uranyl ions from (Karadağ et al., 1995) aqueous solutions. A further enhancement in the uranyl ion uptake of these gels is achieved by pre-structuring them during radiation induced cross-linking process (Akkaş and Güven, 1999).

Adsorptive and binding capacities of acrylamide/maleic acid and acrylamide/itaconic acid based hydrogels were also utilized in the removal of some dyes from aqueous solutions. While pure acrylamide hydrogels showed no adsorption towards a number of basic dyes tested, the presence of diprotic acids in these gels significantly increased their absorptive capacities. The results of batch adsorption studies on some cationic dyes such as basic red, basic green, cresyl violet and basic blue, basic violet from aqueous solutions onto acrylamide/maleic acid (Karadağ et al., 1996b) and acrylamide/itaconic acid (Saraydın et al., 1996) hydrogels have shown the beneficial effect of diprotic acid moieties. The adsorption studies clearly showed that these superswelling hydrogels are potential sorbents to be used for the removal of cationic dyes from wastewaters and aqueous effluents.

The results achieved on bioapplications, heavy metal

ion uptake and removal of dyes from aqueous systems showed that the copolymeric hydrogels prepared from hydrophilic monomers and units with doubly ionizable groups possess some unique properties. Among various methods of synthesis, use of ionizing radiations in the initiation and further cross-linking of starting monomer mixtures seems to provide the best alternative in the preparation of these new class of materials.

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